EXHIBIT 3

_	Protected Information		
560	Page 118		Page 120
1	(Pause.)	1	Q. But my question was more
2	THE WITNESS: I don't	2	pointed. The Mayo Clinic is also highly
3	believe that that is specified.	3	regarded as a referral center for small
4	BY MR. PARKER:	4	bowel disorders, including celiac
5	Q. If you would, please turn to	5	disease.
6	let me see if I can find it.	6	A. Yes.
7	 A. By the way, can we go back 	7	Q. Correct?
8	to where you asked about steroids?	8	A. Uh-hum.
9	Q. Yes, sir.	9	Q. And we can pull it out
10	 I would just point out that 	10	later, but is it your understanding that
11	any patient who makes it to Columbia for	11	what they reported about those 22 people
12	seronegative villous atrophy who has not	12	is that they did not respond to
	responded to a gluten-free diet, steroids	13	immunosuppressants?
14	would be a fairly logical step in their	14	MR. SLATER: Objection.
15	management; and for more or less any	15	You can answer.
16	inflammatory disorder, there is going to	16	THE WITNESS: I really
17	or bothe difficult improvement on ordinar a	17	wouldn't answer that without
18	steroid or an immunosuppressive	18	looking at the paper and that
19	medication, so I think that that could	19	I'd like to look at the paper
20	be true and it decement have any impact on	20	before I say
21	my center that chinesartan was causing	21	MR. PARKER: Let's work
22	their syndrome.	22	through this one, then I promise
23	MR. PARKER: Move to strike.	23	you we will look at the Mayo
24	BY MR. PARKER:	24	paper.
	Page 119		Page 121
1		1	1 460 121
1	Q. Doctor, what you just said	1	BY MR. PARKER:
1 2		1 2	
1020	Q. Doctor, what you just said	2	BY MR. PARKER:
2	Q. Doctor, what you just said is not accurate, however, with regard to	3	BY MR. PARKER: Q. With respect to this paper,
2 3 4	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct?	2 3 4	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of
2 3 4	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct?	2 3 4 5	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia
2 3 4 5	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation.	2 3 4 5 6 7	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite
2 3 4 5 6 7 8	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer.	2 3 4 5 6 7	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that.
2 3 4 5 6 7 8	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it	2 3 4 5 6 7 8	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding
2 3 4 5 6 7 8 9	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how	2 3 4 5 6 7 8 9	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement?
2 3 4 5 6 7 8 9 10	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each	2 3 4 5 6 7 8 9 10	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second.
2 3 4 5 6 7 8 9 10 11 12	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even	2 3 4 5 6 7 8 9 10 11	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure.
2 3 4 5 6 7 8 9 10 11 12 13	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the	2 3 4 5 6 7 8 9 10 11 12	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second
2 3 4 5 6 7 8 9 10 11 12 13	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it	2 3 4 5 6 7 8 9 10 11 12 13 14	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page?
2 3 4 5 6 7 8 9 10 11 12 13 14	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that	2 3 4 5 6 7 8 9 10 11 12 13 14 15	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process. And so if some patients did	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly responsive/refractory CD." That's celiac
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process. And so if some patients did I would expect most patients to	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly responsive/refractory CD." That's celiac disease?
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process. And so if some patients did I would expect most patients to respond to some extent; but if	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly responsive/refractory CD." That's celiac disease? A. Uh-hum.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process. And so if some patients did I would expect most patients to respond to some extent; but if some didn't, that doesn't really	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly responsive/refractory CD." That's celiac disease? A. Uh-hum. Q. So can we agree that all 72
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	Q. Doctor, what you just said is not accurate, however, with regard to the Mayo series of 22 patients who reported not to have responded to steroids; correct? MR. SLATER: Objection; foundation. You can answer. THE WITNESS: I think it depends on I don't know how each group responded how each group defined response; and even if there was a difference in the response, even if you defined it the same way, I would say that there's variation in the disease presentation and the disease process. And so if some patients did I would expect most patients to respond to some extent; but if	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	BY MR. PARKER: Q. With respect to this paper, however, what we're told is that all of these patients were referred to Columbia with a diagnosis of refractory celiac disease; correct? A. That sounds quite reasonable, but let me verify that. Could you tell me where you're finding that statement? Q. Give me one second. A. Sure. Q. Under results, the second page? A. Okay. Q. You'll see the second sentence, "All patients had been referred with a diagnosis of poorly responsive/refractory CD." That's celiac disease? A. Uh-hum.

-	Protected Information -		Steven M. Lagana, M.D.
	Page 122	Г	Page 124
1	either poorly responsive and/or	1	Q. I'm puzzled by the word who
2	refractory celiac disease?	2	were initially found initially labeled
3	 A. I would accept that 	3	with unclassified sprue. We just got
4	statement with a proviso, which is, the	4	done reading where they came to your
5	sentence preceding it states that these	5	Columbia, not your center with
6	were patients with seronegative villous	6	refractory celiac disease. Is that the
7	atrophy, so that means that these	7	same or different than unclassified
8	patients had been serologically tested	8	sprue?
9	for and found to be negative for the test	9	MR. SLATER: Objection.
10	of celiac disease.	10	You can answer.
11	Q. But there is a clinical	11	THE WITNESS: I think the
12	entity of seronegative celiac disease, is	12	problem here is that you're
13	there not?	13	we're a bit conflating what the
14	A. There is.	14	outside physicians thought, which
15	Q. Okay. So these patients	15	with what was thought at
16	were tested to have not to have the	16	Columbia.
17	antibodies typically seen in celiac	17	So the outside physicians
18	disease patients, but nevertheless were	18	said, okay, you've got
19		19	seronegative refractory
20	them to Columbia to have celiac disease	20	nonresponsive celiac disease. And
21	according to what your colleagues wrote	21	from my interpretation of this
22	here.	22	statement and I'll acknowledge
23	MR. SLATER: Objection.	23	that there's a little bit of
24	You can answer.	24	
200	i ou can answer.	55	vagary here these are patients
	Page 123		Page 125
1	THE WITNESS: They were	1	who at Columbia were classified as
2	thought to have a variation, a	2	having unclassified sprue until
3	rare, complicated form of celiac	3	the publication of Rubio-Tapia and
4	disease, yes.	4	
5		1100	then were instead classified as
1 (2)	BY MR. PARKER:	5	olmesartan enteropathy.
6	Q. Thank you.	1100	olmesartan enteropathy. MR. PARKER: Fair enough.
7	Q. Thank you. If you would flip over three	5 6 7	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER:
7 8	Q. Thank you. If you would flip over three pages under the discussion section, which	5	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you
7 8 9	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column	5 6 7 8 9	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with
7 8 9 10	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep.	5 6 7 8 9	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease.
7 8 9 10	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain	5 6 7 8 9 10	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your
7 8 9 10 11	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first	5 6 7 8 9 10 11	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease.
7 8 9 10 11 12	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An	5 6 7 8 9 10 11 12	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told
7 8 9 10 11 12 13	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"?	5 6 7 8 9 10 11 12 13	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory
7 8 9 10 11 12 13 14 15	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum.	5 6 7 8 9 10 11 12 13 14 15	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease.
7 8 9 10 11 12 13 14 15	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in	5 6 7 8 9 10 11 12 13 14 15	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory
7 8 9 10 11 12 13 14 15 16	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who	5 6 7 8 9 10 11 12 13 14 15 16 17	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease.
7 8 9 10 11 12 13 14 15 16 17 18	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified	5 6 7 8 9 10 11 12 13 14 15	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to
7 8 9 10 11 12 13 14 15 16 17 18	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have	5 6 7 8 9 10 11 12 13 14 15 16 17 18	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because
7 8 9 10 11 12 13 14 15 16 17 18 19 20	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have villous atrophy as a result of olmesartan	5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because both of these are rare manifestations of
7 8 9 10 11 12 13 14 15 16 17 18 19 20	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have villous atrophy as a result of olmesartan use.	5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because both of these are rare manifestations of celiac disease and not specifically
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have villous atrophy as a result of olmesartan use. I managed to read that	5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because both of these are rare manifestations of celiac disease and not specifically related, so I'm saying that these
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have villous atrophy as a result of olmesartan use. I managed to read that correctly, did I not?	5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because both of these are rare manifestations of celiac disease and not specifically related, so I'm saying that these patients were thought to have two
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	Q. Thank you. If you would flip over three pages under the discussion section, which is the middle column A. Yep. Q perhaps you can explain this to me: Down towards the first paragraph, do you see where it begins "An interesting finding"? A. Uh-hum. Q An interesting finding in our series was the number of patients who were initially labeled with unclassified sprue who were ultimately found to have villous atrophy as a result of olmesartan use. I managed to read that	5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	olmesartan enteropathy. MR. PARKER: Fair enough. BY MR. PARKER: Q. So the process as you understand it were, patients came in with a label of refractory celiac disease. They got looked at, worked up by your colleagues. A number of them were told A. Seronegative refractory celiac disease. Q. Seronegative refractory celiac disease. A. I'm not making that point to be a jerk. I'm making that point because both of these are rare manifestations of celiac disease and not specifically related, so I'm saying that these

	Protected Information	- " 2	Steven M. Lagana, M.D.
	Page 126		Page 128
1	disease.	1	Q. Do you see the positive
2	Q. Fair enough. And when they	2	
3	came to Columbia initially, they were	3	A. Oh, yes.
4	sent home, some number of them, with a	4	Q I think that's what I was
5	diagnosis of unclassified sprue.	5	looking at. Would that not indicate
6	A. I would agree with the	6	improvement on immunosuppressants?
7	interpretation that you just made.	7	A. As I stated before, any
8		8	inflammatory disease likely to have some
9	changed from seronegative refractory	9	improvement on immunosuppressant. So,
10	celiac disease to unclassified sprue,	10	yes, the interpretation of plus sign
11	/ 100 THE STOCK TO THE TREE TO STOCK TO THE STOCK THE S	11	under IS, or clinical improvement slash
12	그 과 가 가 되는 집에 가 가 되는 그리네다.	12	IS, that indicates that they had some
13	don't have celiac disease?	13	
14	MR. SLATER: Objection.	14	And the following the
15	You can answer.	15	following column indicates that each and
16	THE WITNESS: I'm afraid I	16	every case relapsed after stopping the
17	can't really answer that question.	17	immunosuppressants.
18	MR. PARKER: That's all you	18	Q. So that we understand and
19	can do for me. Okay.	19	is this reflecting the clinical course of
20	BY MR. PARKER:	20	these patients after they came back to
21	Q. Now let's go to table number	21	Columbia when they were contacted and
22	3.	22	는 사람들은 보면 전혀 가는 사는 것이 되었다. 전에 전혀 가는 전에 가장 등에 가장 이렇게 되었습니다. 그 이번 이번 생각이 살고 있었습니다. 그런 사람들은 보다 가장 하나 보다 보다 보다 보다 사람들이 되었습니다. 그런
23	A. Table 3, sure.	23	
24	Q. And you'll see on the	24	A. Maybe you could say it in a
	CONTRACT SELECTION SERVICES CANADAM MACHINE CONTRACT		The same of the sa
	Page 127		Page 129
1	right hand blue of that column, there's a		different way.
2	column labeled "IS"?	2	Q. Sure. You've described that
3	A. Uh-hum.	3	after learning about what the folks in
4	Q. And that would have been	4	the Mayo were going to publish, there was
5	immunosuppressants?	5	an effort to reach out to these 16
6	A. Yes.	6	patients who were found to be taking
7	Q. Would that have been a drug	7	olmesartan and who had been diagnosed
8	indicated for patients diagnosed with	8	man boromegan to contact disease,
9	unclassified sprue?		refractory celiac disease; correct?
10	A. This would be a drug that	10	A. Yes.
(2:20)	you would use for any patient with an	11	Q. And there was some effort to
	inflammatory disorder that you couldn't	0.00	talk to them and get and reconnect
15.18.750757	get under control in a less this is a	13	with morn, and mor round to patients who
0.00	we would consider this sort of a		had been taking olmesartan; correct so
	big-gun drug to introduce to a patient so	1	far?
	that you would you would introduce it	16	A. Yes.
	when other less potentially toxic	17	Q. And some of those patients
1	treatments had failed.	18	came back for further medical follow-up,
19	Q. And we're told that all 16	19	including some had rebiopsies; correct?
20	of these patients had let me get the	20	A. Uh-hum.
	exact words symptomatic improvement;	21	Q. Yes?
2652220	is that correct?	22	A. Yes.
23	A. Can you tell me where you	23	Q. And they were instructed to
24	read those words?	24	stop taking olmesartan.
		i.	

Page 130 Page 132 To the best of my knowledge. Page what, sir? What I'm trying to discern 2 Oh, sorry. Page 4. ³ right now is, when did these 16 patients Okay. O. 4 have their clinical improvements when -- here, you'll see A. 5 they were given immunosuppressants and phraseology that I employ fairly 6 then have relapse when they stopped frequently. To put an exact number on ⁷ taking their immunosuppressants? Was it how many times I've said this, I ⁸ the same time they were told to stop couldn't, but I would say perhaps dozens 9 taking olmesartan? of times. 10 Don't know the answer. 10 So if I have a case in which 11 Q. Okay. Who would we talk to I see the findings described here in the 12 who would know that? report and I don't know whether the 13 A. I would speak to Dr. Green. patient is taking olmesartan, is taking 14 He's the senior author of the paper. -- has had celiac testing, has had some 15 Q. Was he the one running the bone marrow transplant -- if I don't have 16 study? I mean, sometimes senior authors a complete clinical picture, I give a 17 are just senior authors. differential diagnosis, an example of 18 A. I wouldn't -- I wouldn't which is provided here. 19 19 speculate as to how --If you're asking in how many 20 cases have I had the clinical data and we Q. Okay. Fair enough. Okay. 21 Let me put that aside and have come to the conclusion that come back to what I want to discuss olmesartan is the most likely culprit, I before we get visited by lunch. wouldn't be able to put an exact number 24 A. Sure. 24 on it, but not counting the cases that Page 131 Page 133 Q. Doctor, I want to ask you to ¹ I've seen through my work with Mr. ² put aside the plaintiffs, whether ² Slater, you know, more than 10 and less 3 disclosed or undisclosed, that you've than 25 seems to be in the ballpark. 4 been asked by counsel to look at, their Q. And on cases that come to specimens. you in your day-to-day job, not as a 6 Can you give me some idea in litigation consultant, have you ever your world as a practicing pathologist concluded and written in a medical how many reports you've generated in report, this patient has sprue-like which you've concluded in words to the enteropathy associated with olmesartan or 10 effect that the conditions I see in this olmesartan-associated enteropathy or some 11 variation of that term? Have you said patient are consistent with someone 12 this patient has it as opposed to saying taking olmesartan? 13 this is consistent with that? 13 MR. SLATER: Objection. 14 14 You can answer. A. I don't think that I would 15 THE WITNESS: May I refer to ever use those specific words. I think 16 my -- to the report? that those specific words imply a level 17 MR. PARKER: Please. You of clinical detail that rarely is 18 can always refer to anything you available to pathologists at the time of 19 want to look at, Doctor. 19 signing out a case. 20 20 THE WITNESS: Okay. Let us When I've encountered these 21 look at page -- at the bottom of cases, I've given descriptive diagnoses, 22 the first paragraph, the rather 22 like I describe here. I've listed 23 long paragraph -plausible items on the differential 24 BY MR. PARKER: ²⁴ diagnosis, which certainly have included

Page 134 Page 136 olmesartan on a number of occasions, many O. Doctor, we're back on the ² perhaps, and I attempt to follow up that ² record after our lunch break and I want 3 diagnosis with a conversation with the 3 to talk to you for a moment about a 4 clinician. 4 clinical entity we started to talk about If it's a patient being seen 5 before lunch in connection with the --6 at our Celiac Disease Center, it's very 6 how do you pronounce it -- DeGaetani --⁷ likely that that patient would then be paper of unclassified sprue. ⁸ presented in an interdisciplinary A. Uh-hum. ⁹ conference where the gastroenterologists 9 O. Are the terms unclassified 10 and myself and other pathologists would sprue and idiopathic enteropathy 11 discuss the case and we could come to synonymous? 12 that conclusion. 12 A. Idiopathic enteropathy is 13 not a term that I use frequently in my But the words written on a 14 -- you know, on a pathology report, this practice or encounter too frequently in 15 is and can only be olmesartan the literature. Unclassified sprue is 16 enteropathy, that phraseology is unlikely saying someone has a sprue-like illness to make it to a pathology report. and we don't know what the possible 18 Q. In fairness to my question, etiology is, as opposed to, say, celiac 19 I didn't say "and can only be." sprue or olmesartan enteropathy or one of 20 A. Okav. these other sprues where we believe we 21 Q. All right? I just want to know the cause. 22 make sure you're not hedging on me. My 22 So idiopathic enteropathy -question is, have you ever said in a 23 is that term that you used? pathology medical record, this is a case 24 Q. Yes. Page 135 Page 137 ¹ of olmesartan-associated enteropathy or A. -- you know, that to me sprue-like enteropathy? ² doesn't refer to any specific entity. 3 MR. SLATER: Objection: 3 That would be a descriptive term that if 4 asked and answered. I mean, he you used that term in discussion with me, 5 just went through this in detail ⁵ I would take it to mean something similar 6 with you. to unclassified sprue. 7 Q. Okay. Well, if you're more MR. PARKER: He just hedged 8 comfortable with unclassified sprue, I'll 9 MR. SLATER: He didn't hedge use that term for my next area of 10 at all. Come on, Bruce. questions. 11 11 MR. PARKER: Doctor, can you A. Okay. 12 answer my question? Q. Doctor, people today 13 THE WITNESS: I'm sure that continue to get the label of unclassified 14 I've said that I suspected or this sprue; correct? 15 -- you know, this should be 15 A. Yes. 16 16 considered clinically. That's Q. And I can -- can I presume 17 about -- that's probably the correctly that before Benicar, olmesartan 18 strongest phraseology that I would was available in 2002 and people received 19 use in this condition. the diagnosis of unclassified sprue? 20 MR. PARKER: Thank you. 20 A. Uh-hum. 21 21 We'll have some lunch. O. Yes? 22 22 (A luncheon recess was taken A. Yes. 23 23 from 12:36 p.m. to 1:18 p.m.) Q. As you just explained, 24 BY MR. PARKER: ²⁴ doctors diagnose someone with

Page 138 Page 140 unclassified sprue when they present with 1 himself has come to the deposition ² symptoms of enteropathy for which there's 2 room and said this patient has no known cause at that point in time. 3 never touched olmesartan before A. Yes. 4 this developed and then started 5 Q. And for all such people, taking olmesartan after that? Is 6 6 there is some biological reason for them that the situation that you're developing sprue. Medical scientists 7 describing? simply haven't identified what it is. 8 MR. PARKER: Well, I didn't 9 9 MR. SLATER: Objection. invoke God, but I'll make the 10 You can answer. 10 question easier for you. 11 THE WITNESS: I think that BY MR. PARKER: 12 12 what you just said is plausible. Q. Is someone is diagnosed with 13 I would expand on that just a 13 unclassified sprue who has never taken --14 little bit to say that to call and let's just say his doctors say so and 15 someone an unclassified sprue patients say so -- never taken 16 patient means, as you described, olmesartan, they can continue to have 17 we don't know what the cause of unclassified sprue notwithstanding the 18 their sprue is. fact that they're now taking olmesartan. 19 19 It doesn't -- it could mean A. I think that's a possible, 20 -- that could come from one of two although quite rare, scenario, but I do 21 reasons: Either they have a sprue concede that that is a possible scenario. 22 which has a novel cause that we I would also just add to that, we don't 23 don't know or they have sprue due know in those patients if olmesartan 24 to a common cause and we have not could contribute or make -- or exacerbate Page 139 Page 141 1 been able to make the diagnosis ¹ their sprue. For instance, we don't know 2 for whatever reason, so there are in -- there are patients who have -- just 3 based on epidemiology, there are two different ways to get at that certainly patients who have true celiac diagnosis. BY MR. PARKER: disease and who have been prescribed 6 Q. In someone who is diagnosed olmesartan. We don't know if the with unclassified sprue and then starts olmesartan affects those patients taking olmesartan, there's no reason -differently than patients without celiac well, let me rephrase the question. disease. 10 For whatever reasons one may 10 Q. And there's no literature to 11 develop an unclassified sprue, there's no 11 suggest that it does. 12 biologic reason they can't have that and 12 MR. SLATER: Objection. take olmesartan at the same time and be 13 You can answer. 14 14 wholly unrelated to each other. THE WITNESS: Or doesn't. 15 15 MR. SLATER: Objection. MR. PARKER: Let's talk 16 16 You can answer. about the affirmative. Nobody's 17 MR. PARKER: Do you agree? 17 published a paper of any type 18 18 THE WITNESS: I'd like to positing or proposing that a 19 ask you to clarify the question, 19 patient with celiac disease is 20 if I may. Are we talking about a 20 made worse if they start on 21 hypothetical situation in which a 21 olmesartan. 22 patient has signs and symptoms of 22 MR. SLATER: Objection. 23 23 sprue, has a biopsy that shows You can answer. 24 24 sprue-like changes, and God THE WITNESS: There's

1	Page 142		Leven M. Lagana, M.D. 10236
1	nothing in the published	1	Q. And this is one of the
2	literature to that effect yet.	2	papers that was listed in that
3	BY MR. PARKER:	3	supplemental reliance list that we marked
4	Q. Now, going back to my	4	earlier today?
5	question about unclassified sprue, it is	5	A. Uh-hum.
6	reported in the literature that patients	6	Q. Okay?
7	T 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	7	A. Yes.
8	of them spontaneously resolve.	8	Q. And it is not one that is
9	Have you seen that in the	9	referenced in any manner in your report;
10	literature?	10	correct?
11	A. That sounds familiar, but	11	A. That's correct.
12	before I agree to that point, I'd like to	12	Q. Have you read this paper
13	if you have something with you that	13	before coming to the deposition today?
	documents that, I'd like to confirm that.	14	A. I have.
15		15	Q. It is a it was, as
16	 Q. Sure, sure. Have you ever seen that in 	16	described, a prospective study over,
17	your clinical practice, of patients with	17	what, 15 years, 10-plus years?
18	diagnosed unclassified sprue resolving	18	A. It looks like 15 years.
19	spontaneously, or has it been reported to	19	Q. Okay. And it was an attempt
20		20	by these investigators to collect cases,
21	A. And for the purposes of this	21	as we discussed previously, of
22	question, we're excluding the cases seen	22	seronegative villous atrophy?
23	at Columbia who were thought to be	23	A. Yes.
	unclassified and later categorized as	24	Q. And in this report, they
	KERNORINEROK INGRAN DICTORIO DORI. CONPUTARRIO CARLO NERO CONSULA PER SIGNA DICTORRANDO NI CINTRA		Q. And in this report, they
	Page 143		Page 145
1	olmesartan?		describe various causes that they
2	Q. Yes, I'm not involving		attribute to these patients, which are
3	olmesartan at all.	3	C
			reflected in figure number 2, the pie
4	 A. Okay. I don't remember a 	4	chart?
5	case, but I don't think it sounds		chart? A. Figure 2. Okay.
5 6		4 5 6	chart? A. Figure 2. Okay. Q. Do you see that, Doctor?
5 6 7	case, but I don't think it sounds unreasonable.	4 5 6 7	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do.
5 6 7 8	case, but I don't think it sounds unreasonable. (Deposition Exhibit No.	4 5 6 7 8	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked
5 6 7 8 9	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article	4 5 6 7 8	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed
5 6 7 8 9	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical	4 5 6 7 8 9	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had
5 6 7 8 9 10	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous	4 5 6 7 8 9 10	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is
5 6 7 8 9 10 11	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre	4 5 6 7 8 9 10 11	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right?
5 6 7 8 9 10 11 12	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult	4 5 6 7 8 9 10 11 12 13	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading
5 6 7 8 9 10 11 12 13	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period	4 5 6 7 8 9 10 11 12 13	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that.
5 6 7 8 9 10 11 12 13 14	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was	4 5 6 7 8 9 10 11 12 13 14 15	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie
5 6 7 8 9 10 11 12 13 14 15 16	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period	4 5 6 7 8 9 10 11 12 13 14 15 16	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200
5 6 7 8 9 10 11 12 13 14 15 16	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.)	4 5 6 7 8 9 10 11 12 13 14 15 16 17	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded
5 6 7 8 9 10 11 12 13 14 15 16 17	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER:	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous
5 6 7 8 9 10 11 12 13 14 15 16 17 18	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER: Q. Doctor, Exhibit 6 is a copy	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous atrophy?
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER: Q. Doctor, Exhibit 6 is a copy of the study by Drs. Aziz and others,	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous atrophy? A. I see that.
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER: Q. Doctor, Exhibit 6 is a copy of the study by Drs. Aziz and others, which your colleague, Peter Green, is a	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous atrophy? A. I see that. Q. And then there was a group
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER: Q. Doctor, Exhibit 6 is a copy of the study by Drs. Aziz and others, which your colleague, Peter Green, is a co-author on.	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous atrophy? A. I see that. Q. And then there was a group of 36, or 18 percent, that they describe
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	case, but I don't think it sounds unreasonable. (Deposition Exhibit No. Lagana-6, 2016 Original Article "The clinical and phenotypical assessment of seronegative villous atrophy; a prospective UK centre experience evaluating 200 adult cases over a 15-year period (2000-2015)" by Aziz, et al, was marked for identification.) BY MR. PARKER: Q. Doctor, Exhibit 6 is a copy of the study by Drs. Aziz and others, which your colleague, Peter Green, is a	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	chart? A. Figure 2. Okay. Q. Do you see that, Doctor? A. I do. Q. And they specifically asked a question to themselves as they reviewed these cases of whether the patients had been exposed to any form of an ARB; is that right? A. I believe I recall reading about that. Q. And if you look at the pie chart, they report in this group of 200 that there were 13 that they concluded had a drug-induced seronegative villous atrophy? A. I see that. Q. And then there was a group

	Protected Information		Steven M. Lagana, M.D.
	Page 146		Page 148
1	A. I do.	1	paper?
2	Q. And if you look on page 5,	2	A. I think that I think that
3	Doctor, the same page as the pie chart	3	perhaps this came to my attention either
4	excuse me on the right-hand column, do	4	through the defense expert reports or
5	you see the paragraph beginning,	5	from Mr. Slater. I don't recall
6	"Finally, in 36 cases"?	6	precisely.
7	A. Uh-hum.	7	Q. But relatively recently
8	 Q. And I'm going to paraphrase, 	8	 Relatively recently, yeah.
9	but you tell me if I misstate this, what	9	Q. When you did have it brought
10	they're saying. They looked at these 36	10	to your attention in one of those two
11	cases of seronegative nonceliac disease	11	ways and you saw that your senior
12	and report that they were unable to	12	colleague, Peter Green, was an author,
13	attribute any cause after looking for	13	have you ever walked down to his office
14	drug induced reasons; and they report	14	and asked him about this paper?
15	that 26, or 72 percent, had spontaneous	15	 I have not spoken to him
16	recovery by evidence of duodenal biopsy?	16	about this paper.
17	 I see that, yep. 	17	 Q. Have you ever had a
18	Q. Is this then an example in	18	conversation with Peter Green or some of
19	the literature of patients they used	19	the other senior gastroenterologists
20	the term "idiopathic enteropathy" as	20	about spontaneous remission of
21	we discussed, people with enteropathy of	21	unclassified sprue?
22	unknown causes, medications being	22	 A. You know, I can't recall a
23	considered, that resolved spontaneously?		specific instance.
24	 A. That is what this group 	24	 Q. Doctor, putting aside the
Г	Page 147		Page 149
		1	1 age 149
1	reports, so I would agree that this group	1	
1 2		1 2	history of olmesartan, what clinical
2	reports, so I would agree that this group	535	history of olmesartan, what clinical features as reported in the literature or
2	reports, so I would agree that this group has reported some examples of that. I	2	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified
3	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the	2	history of olmesartan, what clinical features as reported in the literature or
2 3 4	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the	2 3 4 5	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to
2 3 4	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy	2 3 4 5	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with
2 3 4 5 6	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A so that really is a	2 3 4 5 6	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan?
2 3 4 5 6 7	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are	2 3 4 5 6	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would
2 3 4 5 6 7 8 9	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their	2 3 4 5 6	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the
2 3 4 5 6 7 8 9 10	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug.	2 3 4 5 6 7 8 9 10	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it.
2 3 4 5 6 7 8 9	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is	2 3 4 5 6 7 8 9 10 11	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well
2 3 4 5 6 7 8 9 10 11 12 13	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that	2 3 4 5 6 7 8 9 10 11 12 13	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection.
2 3 4 5 6 7 8 9 10 11 12 13 14	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or	2 3 4 5 6 7 8 9 10 11 12 13	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over
2 3 4 5 6 7 8 9 10 11 12 13 14 15	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions	2 3 4 5 6 7 8 9 10 11 12 13 14	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve some	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve —	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously. A. According to this case	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of unclassified sprue, no.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously. A. According to this case series, this is — this case series has	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of unclassified sprue, no. MR. SLATER: Oh,
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously. A. According to this case series, this is — this case series has shown some examples of that.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of unclassified sprue, no. MR. SLATER: Oh, unclassified sprue.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously. A. According to this case series, this is — this case series has shown some examples of that. Q. And when you — can you give	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of unclassified sprue, no. MR. SLATER: Oh, unclassified sprue. MR. PARKER: Yes.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	reports, so I would agree that this group has reported some examples of that. I would add that this is made after the exclusion of a drug-induced enteropathy Q. Yes, sir. A. — so that really is a different group of patients than the olmesartan enteropathy patients who are diagnosed, in large part, based on their response to cessation of the drug. Q. My question, however, is that what this is reporting is that people who have unclassified sprue or idiopathic enteropathy, those conditions of unknown causes do resolve — some number of them do resolve — spontaneously. A. According to this case series, this is — this case series has shown some examples of that.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	history of olmesartan, what clinical features as reported in the literature or through your training of unclassified sprue are different in any respects to sprue-like enteropathy associated with olmesartan? A. The main differences would be exposure to olmesartan and improvement upon cessation of olmesartan. Q. But my question was the clinical features of it. A. Well MR. SLATER: Objection. This is are you going back over this? Unless I'm misunderstanding. Didn't we go over this MR. PARKER: Not of unclassified sprue, no. MR. SLATER: Oh, unclassified sprue.

Page 150 Page 152 unclassified sprue, you can see a presentation, all with the same drug 2 range of findings similar to what ² exposure, that the intervention of 3 we discussed with olmesartan 3 removing the drug would cause spontaneous 4 enteropathy. And I can't --4 resolution of a totally unrelated 5 you're asking if there's a condition so consistently. 6 specific clinical feature that's So I think that -- and of 7 different in one versus the other? course there are rechallenges, there are 8 MR. PARKER: Yes, I'm -rechallenges in the literature. I 9 reviewed a number of cases in which yes. 10 THE WITNESS: Okay. Simply patients were rechallenged and the 11 the history of olmesartan symptoms returned, quickly in a lot of 12 exposure. 12 cases. 13 BY MR. PARKER: 13 So I think that, you know, 14 O. Okay. Put aside whether the we are making determinations to a 15 person used drug. In their symptoms, reasonable degree of medical certainty, their clinical -- I mean their findings, but I would think beyond that, the idea when you take their blood, when you do that all -- that all or most of these all the stuff that doctors do to someone. patients had unclassified sprue and just is there anything that you can say, you happened to get better totally unrelated know, that happens with people with to the cessation of olmesartan, that's, unclassified sprue, it doesn't happen you know, astronomical. The odds against with olmesartan or vice versa? 22 that are astronomical. 23 MR. SLATER: Objection. 23 Q. But that wasn't my question. 24 You can answer. ²⁴ My question was, have you ever had that Page 151 Page 153 1 THE WITNESS: I don't ¹ discussion with your colleagues as to how 2 believe so. can we determine whether or not in a BY MR. PARKER: given patient -- if they happen to get Q. Doctor, have you ever had a better some period of time after we 5 discussion with your colleagues at discontinue olmesartan, how can we be 6 Columbia on the following issue: Have sure that the olmesartan was the reason you ever been a participant in discussion as opposed to a spontaneous resolution of that's asked the question, in someone --8 the symptoms? Have you had the how do we know in someone who has discussion, is all I'm asking. 10 unclassified sprue and who happens to be A. We've had the discussion in 11 taking olmesartan that it is the relation to individual patients. I don't 12 olmesartan cessation that is a result of 12 think that we've had it -- you know, I them getting better rather than don't remember anyone pounding the table spontaneous remission of the unclassified and saying, no, no, this is unrelated. 15 sprue? 15 How could you prove to me that -- the 16 A. Well, in some cases, these change was so dramatic in these patients, 17 patients have suffered for years and the as they report, based on the cessation of cessation of olmesartan on a time scale, the drug, that there wasn't really much 19 although sometimes it can take awhile to pushback against that explanation. But 20 heal, often these patients feel better it was certainly discussed. even within days. 21 Q. And the Aziz paper is not 22 the only paper in the literature that So it would seem unlikely 23 that in a bunch of patients with somewhat talks about unclassified sprue or 24 variable, but some similarities in their ²⁴ idiopathic enteropathy patients resolving

	Protected Information -		Page 156
1	spontaneously, is it?	1	Page 156
2	A. I would certainly presume	2	A. Okay.
3	not, but as we said before, I would like	3	Q. And this is a paper on your supplemental reliance list; correct?
4	to see the specific examples that you're	4	A. Yes.
5	referring to.	5	Q. Can I assume that since it's
6	Q. Why don't you pull out your	6	on your reliance list, that you've read
7	supplemental reliance list, sir, please.	7	it?
8	A. Okay.	8	A. I have read it.
9	Q. You have it I'm sorry.	9	Q. And would this have been one
10	It should be Exhibit 4?	10	that came to you relatively recently,
11	A. Okay.	11	like the Aziz study?
12	Q. Here (Indicating) it is.	12	A. Sorry. What's that?
13	A. Okay.	13	Q. Like the Aziz study.
14	Q. Is there one on your	14	A. I saw this several months
15	supplemental reliance list that talks	15	ago. Yeah, I I believe I
16	about spontaneous resolution of	16	Histopathology is one of the journals
17	unclassified sprue?	17	
18	MR. SLATER: Is the question	18	me every month, so I believe I saw this
19	whether that's the title of the	19	when it came out and I looked at it again
20	article?	20	in preparation for the deposition.
21	MR. PARKER: No. Does one	21	Q. Okay.
22	of these papers address that	22	It was not studied, however,
23	topic?	23	for purposes of writing your general
24	MR. SLATER: Objection.	24	causation report.
	PRODUCTOR OF THE PROPERTY OF T	_	Control of the second s
1	Page 155	1	Page 157
1 2	THE WITNESS: I think that	1 2	A. Correct.
2	THE WITNESS: I think that if there's a paper in mind that	2	A. Correct.Q. Okay. Now, this is a paper
	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm	2	A. Correct.Q. Okay. Now, this is a paper and this is a pretty good journal, is
2 3 4	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking	2	A. Correct.Q. Okay. Now, this is a paper and this is a pretty good journal, is it not?
3	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you	2	 A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree.
2 3 4 5	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was	2 3 4 5	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste
2 3 4 5	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think	2 3 4 5	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right?
2 3 4 5 6 7	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not	2 3 4 5 6 7	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in
2 3 4 5 6 7 8	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard.	2 3 4 5 6 7 8	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good
2 3 4 5 6 7 8	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I	2 3 4 5 6 7 8 9	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal.
2 3 4 5 6 7 8 9	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess.	2 3 4 5 6 7 8 9 10	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay.
2 3 4 5 6 7 8 9 10	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I	2 3 4 5 6 7 8 9 10 11	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a
2 3 4 5 6 7 8 9 10 11	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay.	2 3 4 5 6 7 8 9 10 11 12 13	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as
2 3 4 5 6 7 8 9 10 11 12	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay.	2 3 4 5 6 7 8 9 10 11 12 13 14	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks
2 3 4 5 6 7 8 9 10 11 12 13	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited")	2 3 4 5 6 7 8 9 10 11 12 13 14 15	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac.
2 3 4 5 6 7 8 9 10 11 12 13 14	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown,	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown, et al, was marked for	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or idiopathic enteropathy or is this yet
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown,	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or idiopathic enteropathy or is this yet another label that we have to put on a
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown, et al, was marked for identification.)	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or idiopathic enteropathy or is this yet another label that we have to put on a clinical syndrome?
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown, et al, was marked for identification.)	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or idiopathic enteropathy or is this yet another label that we have to put on a clinical syndrome? MR. SLATER: As opposed to
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	THE WITNESS: I think that if there's a paper in mind that you'd like me to look at, I'm happy to do so. If you're asking me to remember the detail you know, whether that detail was included in any of these, I think that's a bit I would not venture a guess in that regard. MR. PARKER: Okay. And I don't want you to guess. THE WITNESS: Okay. (Deposition Exhibit No. Lagana-7, 2015 Paper "Self-limited coeliac-like enteropathy: a series of 18 cases highlighting another coeliac disease mimic" by Brown, et al, was marked for identification.) BY MR. PARKER: Q. Let me hand you Exhibit No.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	A. Correct. Q. Okay. Now, this is a paper and this is a pretty good journal, is it not? A. I agree. Q. I assume you wouldn't waste your time reading bad journals. Right? A. I have published in Histopathology. I think it's a good journal. Q. Very good. Okay. And this is describing a series of 18 people who have, as described here, enteropathy that looks like celiac, but is not celiac. A. Correct. Q. And is that deserving of the moniker of unclassified sprue or idiopathic enteropathy or is this yet another label that we have to put on a clinical syndrome?

	FIOCECCEG INIOIMACION -	00	steven M. Lagana, M.D.
-	Page 158		Page 160
1	what they caned it.	1	by imptoring fusiced, diffees you found
2	TILL WITHESS. Tean, Tinean,	2	that someplace which I haven't
3	I don't think that they expressly	3	seen it.
4	labeled these patients as	4	So I would say that there is
5	unclassified sprue unless	5	some similarity here to a
6	perhaps if you recall that they	6	sprue-like illness, but I don't
7	did, I'm open to reconsidering	7	think that they're exactly the
8	that statement, but I don't	8	same.
9	remember them labeling them in	9	BY MR. PARKER:
10	that way.	10	Q. Have you ever seen a patient
11	This paper you know, this	11	
12	is a study that was done in	12	
13	Australia and it looks like 66	13	any of these his patient?
14	percent of their patients were	14	MR. PARKER: No. Have you
15	thought to be infectious. The	15	ever seen a patient with these
16	infections that they encounter in	16	type of symptoms in his clinical
17	Australia could certainly be	17	practice.
18	different than the infections that	18	MR. SLATER: Objection.
19	we encounter here.	19	You can answer.
20	I mean, I I acknowledge	20	THE WITNESS: I have seen
21	this paper. I don't dispute their	21	patients with acute onset of
22	the generalities of it. I	22	symptoms and with histology that
23	would probably leave my assessment	23	looks like this. I don't I
24	at that, unless you'd like to talk	24	don't recall any in which I had
_	Page 159		Page 161
1	about it more.	1	the extent of clinical information
2	MR. PARKER: I'm not sure	2	that they had here, so I couldn't
3	that was my question.	3	say if I have seen patients that,
4	BY MR. PARKER:	4	you know, fall entirely within the
5	Q. But my question now is, as	5	spectrum of what they're reporting
6	you read this paper, the clinical	6	here.
	condition that's being described, is it	7	BY MR. PARKER:
8	describing an unclass a patient	8	Q. And in an effort to try to
9	population of unclassified sprue?	9	understand why these patients had this
10	MR. SLATER: Objection.	10	clinical presentation, they describe a
11	You can answer.	11	number of different reasons, one of which
12	THE WITNESS: Okay. I would	12	are medication medication-associated
13	need to refresh myself.	13	enteropathies, including olmesartan.
14	MR. PARKER: Take a look at	14	MR. SLATER: Objection.
15	it, please.	15	That's foundation, actually.
16	THE WITNESS: Okay.	16	There's an issue with what you
	(Pause.)	17	just said.
17		- III	But you can go ahead.
17 18	580 ACCOMMON	18	
	THE WITNESS: Well, to	18	
18	THE WITNESS: Well, to diagnose someone with a sprue-like		THE WITNESS: Sorry. I can
18 19	THE WITNESS: Well, to diagnose someone with a sprue-like illness, I would want to see some	19	THE WITNESS: Sorry. I can answer?
18 19 20	THE WITNESS: Well, to diagnose someone with a sprue-like illness, I would want to see some chronicity to it. Here, they	19 20 21	THE WITNESS: Sorry. I can answer? MR. SLATER: You can answer.
18 19 20 21	THE WITNESS: Well, to diagnose someone with a sprue-like illness, I would want to see some chronicity to it. Here, they describe that all of the cases had	19 20 21 22	THE WITNESS: Sorry. I can answer? MR. SLATER: You can answer. THE WITNESS: Okay, Yes.
18 19 20 21 22	THE WITNESS: Well, to diagnose someone with a sprue-like illness, I would want to see some chronicity to it. Here, they	19 20 21	THE WITNESS: Sorry. I can answer? MR. SLATER: You can answer.

	Protected Information Page 162		Page 164
1	out and they did according to them	1	spontaneously. That's all.
2	rule those out; correct?	2	A. I appreciate it and
3	A. Yep.	3	Q. Okay.
4	Q they were left with 18	4	Has this discussion jogged
5	patients, 10 of whom were said to have	5	your memory of any other papers that
6	resolution of all their symptoms within	6	you've read in the literature of
7	one month of the onset. I'm sorry.	7	enteropathies not associated with
8	That's under results (Indicating).	8	medications that resolved spontaneously?
9	 A. Most within two weeks 	9	A. I'd like to just take a bit
10	okay. Yes, I see that now.	10	of to clarify your language a little
11	Q. Putting aside whether you	11	bit. You said any other enteropathies
12	would fit these people into the rubric of	12	that resolved spontaneously. These
13	unclassified sprue or something else,	13	patients in the Brown paper, I don't
14	here we have yet another grouping of	14	classify as as an unclassified sprue
15	patients with small bowel symptoms who	15	patient or this is a different cohort
6	are said to have resolved spontaneously.	16	of patients. I just want to in my
17	A. With a different set of	17	opinion, this is a much different cohort
18	symptom symptoms that last two weeks	18	of patients. I don't put them in the
19	are different than symptoms that last two	19	same category as, say, the DeGaetani
20	months or two years, so I would actually	20	paper.
21	think now that I've seen that bit of	21	MR. PARKER: Okay. I move
22		22	to strike.
23		23	
24	olmesartan enteropathy patients than	24	Q. That wasn't my question. My
	Page 163		
1	they're very different patients.	1	Page 165 question was enteropathy. I used that
2	And the other thing I noted		
3	when I looked at this is that some of	3	You're not going to fuss
4		4	with me that these people don't have
5	patient that's 2, a patient who's 9, a		enteropathies, are you?
	number of patients in their 30's, their	6	MR. SLATER: Objection to
	20's.	7	the form.
8	So this really to me is a	8	You can answer.
9	different set of patients on a different	9	THE WITNESS: If we're
LO	continent with different exposures to	10	defining enteropathy just as
1	viral pathogens, bacterial pathogens. If	11	inflammation and changes to the
	you're asking me will I grant the broad	12	villi with no without taking
	point that some patients who have villous	13	into account any clinical
	atrophy and inflammation on biopsy can	14	variables, then I'll not fuss with
	resolve on their own, yes, I grant that	15	you about that.
	point.	16	MR. PARKER: I was using
7	I think that this is a very	17	your definition. That's why I
	different set of patients, though, than	18	asked you that at the outset of
9	the ones that we're talking about in the	19	the deposition.
12.5	group of olmesartan	20	
0	ELVIOLUT VII VIIII VANILIZIII ==		THE WITNESS: Well, I used a
	1754 C C C C C C C C C C C C C C C C C C C	21	broad
1	Q. I was simply trying to	21 22	broad
21	Q. I was simply trying to respond to your invitation that I share	22	MR. SLATER: Okay. One
1 2 3	Q. I was simply trying to	755	

	Protected Information	- 2	Steven M. Lagana, M.D.
	Page 166		Page 168
1	question. All he did was make a	1	So 20 of the 22 patients had
2	statement to you.	2	been given that steroid and had not had,
3	BY MR. PARKER:	3	in their words, any apparent clinical
4	 Q. As you defined enteropathy 	4	benefit?
5	at the beginning of this deposition,	5	 I agree with that, yeah.
6	these people have enteropathies.	6	 We had just discussed that.
7	MR. SLATER: Objection.	7	So I wanted to give you my reference.
8	You can answer.	8	That's all.
9	THE WITNESS: Can I have it	9	A. Okay.
10	read back to me?	10	Q. Now would you please turn to
11	MR. PARKER: From four hours	11	table 3 on the last page?
12	ago, I don't think we're going to	12	A. Okay.
13	spend the time, so I'll move on if	13	Q. Actually, second to the last
14	you don't remember your	14	page
15	definition.	15	A. I would, by the way
16	THE WITNESS: Okay.	16	clinical benefit, I would like to if I
17	MR. PARKER: Okay.	17	had them here to question, I'd like to
18		18	know exactly what they meant by clinical
19	(Deposition Exhibit No.	19	benefit. That's a bit vague.
20	Lagana-8, 2012 Original Article	20	Q. Well, and so is improvement.
21	"Severe Spruelike Enteropathy	21	so what is chinear improvement, sir.
22	Associated With Olmesartan" by	22	 Clinical improvement would
23	Rubio-Tapia, Murray, et al, was	23	depend on what the presenting problem
24	marked for identification.)	24	was.
-	Page 167		Page 169
1		1	Q. Okay.
2	BY MR. PARKER:	2	A. If it is someone with
3	Q. Let's move on to Exhibit No.	3	diarrhea and weight loss, improvement
4	8, which is the Mayo Clinic 2012 paper.	4	would be less diarrhea. At the least
100,000	And I'd like you to turn, please, to	(21%)	the least improvement would be a slowing
6	well, first, we had a discussion before		of the rate of weight loss. Better would
7	about resolution who are not on steroids.		be less would be weight stabilization
8	You recall that?	8	and best would be weight gain.
9	 A. I do and I recall pointing 	9	Q. One term that we have talked
10	out the difference between improvement	10	about, but I didn't ask you to define at
11	and resolution.	11	the outset, was diarrhea. What's a
12	Q. Right. And just see if we	12	medical your working medical
13	can agree on our reading of what is said	13	definition of diarrhea?
14	here. If you would turn to page 735	14	A. That's funny. It's a term
15	A. Okay.	15	that we learn in first year of med school
16	Q in the section labeled	16	and then no one asks you to define again.
17	"Treatment and Subsequent Course," the		Frequent, watery stool.
18	authors write: Most of the patients in	18	Q. What is considered to be a
19	our study had undergone several	19	normal number of bowel movements a day?
20	therapeutic trials without apparent	20	A. There is a standard that
21	clinical benefit before referral to Mayo	21	I've seen in the literature. I don't
3809	Clinic, including the use of gluten-free		remember offhand.
	diet for months, systemic corticosteroids	23	Q. What is your understanding
24	and/or budesonide, N equals 20.	24	or how you well, strike that.

	d-020 Protected Information	- K	reeven in Lagana, in.b.
es	Page 170	-	Page 172
1	Do you ever use the term	1	Q. Are you in agreement with
2	"chronic diarrhea"?	2	the folks at the Mayo that what they list
3	A. Yes.	3	here are the clinical features of
4	Q. What does chronic diarrhea	4	sprue-like enteropathy associated with
5	mean?	5	olmesartan?
6	 A. Chronic diarrhea is diarrhea 	6	MR. SLATER: Objection;
7	that lasts more frequently than not for a	7	foundation.
8	month or more.	8	You can answer.
9	Q. Okay. With those	9	THE WITNESS: I believe that
10	definitions in mind then, let's turn to	10	they're listing the most common or
11	table number 3.	11	most the features that struck
12	A. Table 3, sure.	12	them mostly in their original
13	Q. And here we see the folks at	13	series of 22 patients.
14	the Mayo Clinic who first report well,	14	BY MR. PARKER:
15	let me ask you, this was the group that	15	 Q. My question is, do you agree
100	first reported this enteropathy that's	16	with it?
17	associated with that was associated	17	MR. SLATER: Objection.
18	with olmesartan in this paper.	18	You can answer.
19	 A. The same group did make 	19	THE WITNESS: Okay.
20	reference to this. They made a vague	20	I think these are some, but
21	reference to it in an earlier paper which	21	not all, of the features.
200	was on collagenous sprue, if I remember	22	BY MR. PARKER:
23	torretary, where they member that a	23	Q. And what other features
24	fairly significant number of the	24	would you put in such a table listing the
	Page 171	+	
	rage 171		Page 173
1	collagenous sprue patients were taking	1	Page 173 clinical features of sprue-like
11.000	10 To	1 2	72
11.000	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort	100.00	clinical features of sprue-like
3 4	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this	2	clinical features of sprue-like enteropathy associated with olmesartan?
2 3 4 5	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the	3	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer.
2 3 4 5	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this	3 4	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked
2 3 4 5	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the	2 3 4 5 6 7	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of
2 3 4 5 6 7 8	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right?	2 3 4 5 6 7 8	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so
2 3 4 5 6 7 8 9	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes.	2 3 4 5 6 7 8	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go
2 3 4 5 6 7 8 9	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia.	2 3 4 5 6 7 8 9	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal
2 3 4 5 6 7 8 9 10	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes.	2 3 4 5 6 7 8 9 10	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea,
2 3 4 5 6 7 8 9 10 11	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge,	2 3 4 5 6 7 8 9 10 11	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I
2 3 4 5 6 7 8 9 10 11 12 13	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia	2 3 4 5 6 7 8 9 10 11 12 13	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact
2 3 4 5 6 7 8 9 10 11 12 13 14	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they	2 3 4 5 6 7 8 9 10 11 12 13 14	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those
2 3 4 5 6 7 8 9 10 11 12 13 14	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that	2 3 4 5 6 7 8 9 10 11 12 13 14 15	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome. A. Well, I can I certainly	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea and vomiting. We've seen patients
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome. A. Well, I can I certainly did not and no one else voiced that to me	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea and vomiting. We've seen patients with pain, abdominal pain. We've
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome. A. Well, I can I certainly did not and no one else voiced that to me that I recall.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea and vomiting. We've seen patients with pain, abdominal pain. We've seen patients with fatigue. There
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome. A. Well, I can I certainly did not and no one else voiced that to me that I recall. Q. Fair enough. Okay. Now	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea and vomiting. We've seen patients with pain, abdominal pain. We've seen patients with fatigue. There are case reports with bowel
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	collagenous sprue patients were taking olmesartan. But if I recall, they didn't draw any direct conclusions. It was sort of a passing observation; whereas, this paper really establishes the case the clinical characteristics. Q. And you were a resident in 2010 when that paper came out. Right? A. Yes. Q. At Columbia. A. Yes. Q. And to your knowledge, neither you nor anybody else at Columbia drew the conclusion that when they described the six or so patients in that paper on collagenous sprue, that they were describing a different and new clinical syndrome. A. Well, I can I certainly did not and no one else voiced that to me that I recall.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	clinical features of sprue-like enteropathy associated with olmesartan? MR. SLATER: Objection. You can answer. It's asked and answered, but you can answer. THE WITNESS: Well, I think I would actually voice a number of points of contention with this, so we can start with let's just go down the list gastrointestinal symptoms (e.g. chronic diarrhea, weight loss, and steatorrhea), I agree particularly with the fact that it's labeled e.g., so those are some examples. Those are not every example. I would also mention that we've seen patients with nausea and vomiting. We've seen patients with pain, abdominal pain. We've seen patients with fatigue. There

Page 174 Page 176 1 certainly dehydration, kidney that that's necessary. 2 damage. Celiac disease testing, 3 And so I've just listed some there are two points here that -- well, 4 additional examples for the e.g. really three points -- that relate to 5 part. I'm not even -- I wouldn't celiac disease testing. I think it's 6 swear that I've listed every good to know. I think it's reasonable to 7 possible symptom, but I listed do in any patient that you're suspecting 8 some that I'm familiar with. olmesartan-associated enteropathy, but I BY MR. PARKER: don't think it's required for the 10 Q. And those symptoms you are 10 diagnosis. 11 telling me are not just symptoms that 11 And, furthermore, the biopsy happen to appear in patients, but are, in findings are characteristic, but I don't fact, symptoms that are characteristic of think that they are absolutely required 14 enteropathy associated with olmesartan. for the diagnosis. 15 15 Yes, in my opinion. Q. So my questions have been 16 Q. I mean, for example, Doctor, are there any other clinical features as 17 someone could have an enteropathy and outlined here with which you agree -happen to have cancer also and if -- they disagree, and I know you've given me a could have cancer of the bowel, but full answer. I'm not going back over the you're not going to tell me cancer of the 20 gastrointestinal symptoms. bowel is a feature of sprue-like 21 A. Okay. 22 enteropathy, are you? O. Are there any other clinical 23 MR. SLATER: Objection. features as outlined here that you 24 You can answer. disagree with and say this is not part of Page 175 Page 177 1 THE WITNESS: If I felt that this syndrome or you need to add to? 2 cancer of the bowel was more That's what I'm not hearing. 3 common in patients on olmesartan, Because most of these are 4 which I don't, I have no reason to negative findings. They're saying 5 think that, but if I thought that, exclude this, that, and the other, 6 then I would list it as a possible negative IgA/tTG antibody test --7 feature. Q. Is that required? 8 But in the real world, no, I A. No, not in my opinion. 9 don't think that there is a cancer So you don't have to rule 10 association. 10 that out. 11 BY MR. PARKER: 11 A. 12 12 Q. Let's continue on the chart Okay. Do you have to rule 13 then. What else do you have issue with? out lack of a clinical response to 14 A. I think that this chart is gluten? 15 very appropriate for when we're first 15 A. No. 16 16 learning about a disease. I think in Q. Do you have to rule out 17 clinical practice now, the only one of 17 other causes of enteropathy before you 18 these that I think is really paramount is diagnose someone with sprue-like 19 evidence of clinical improvement after 19 enteropathy associated with olmesartan? 20 suspension of olmesartan. A. No. 21 Histologic improvement, I 21 And if I understood your 22 would not -- I would not demand that. last answer, the only thing that you 23 That involves an additional invasive absolutely require for the diagnosis is some clinical report of some improvement ²⁴ procedure for a patient. I don't think

Page 178 Page 180 in one or more of the symptoms. tests, they could miss a case of 2 A. That's the key feature. I actual celiac disease, absolutely. 3 would -- if I may --3 So it's not what I would 4 Q. Sure. describe as -- there's a 5 A. -- I'm not saying none of 5 difference between what's ideal 6 these things add to the picture or none 6 and what's reasonable, and there 7 of these things are helpful or none of 7 are different discussions that 8 these things are rational to do. I think 8 could happen around either of they're all perfectly rational to do. 9 those. 10 But I think that if a 10 MR. PARKER: Or the standard patient had a symptom that a trained 11 of care. gastroenterologist thought might be 12 MR. SLATER: Objection. 13 related to their olmesartan and the THE WITNESS: As it's gastroenterologist told the patient to 14 developing. get off the olmesartan and they did and BY MR. PARKER: 16 they improved, I don't think it would be Q. Doctor, you made the unreasonable at all for that statement in your report -- I'll refer to gastroenterologist to presume or to page 5 of your report, and that report is conclude, I should say, that the Exhibit No. 3 -- that the folks at the 20 olmesartan was the cause of their injury. Mayo Clinic, to use your words, were 21 Q. And your statement necessarily conservative -- that's your 22 word. presupposes, does it not, that there are not other confounding treatments going on 23 A. Okay. with that patient, such as drugs being -- when they wrote in their Page 179 Page 181 given that either are known to induce paper that the evidence that they had diarrhea or drugs that are being given amassed was not proof of causation. that are designed to stop diarrhea? Do you recall that -- or do 4 MR. SLATER: Objection. you see it in your report? Page 5, 5 two-thirds of the way down. You can answer. 6 THE WITNESS: There are a A. Yep. Yeah, and --7 lot of suppositions in what I just Q. What's the basis for your 8 said to you, including, I'll say statement, sir -- I just wanted to have 9 you directed to that -- what's the basis again, that all of these things 10 are reasonable and rational things for your statement that these authors, 11 when they wrote that their evidence did 11 to do. We're talking about the 12 12 not prove causality, that they were absolute requirement. 13 13 I think if a patient came in being, quote, necessarily conservative? 14 14 with complaints that were A. Well, this was the first 15 associated with -- that could be major description of an association 16 associated with olmesartan and between olmesartan and enteropathy. So 17 as we discussed before, associations can enteropathy and the 18 gastroenterologist did nothing be spurious or they can be causative and 19 except stop olmesartan, didn't do I think when you have just one case 20 any of these things, it's likely series, you know, there were not a 21 that they would -- they would have hundred different cases in the literature 22 a decent chance of being wrong, 22 at this point, the strength of causality 23 the patient might have celiac was not -- the association was not as 24 disease. If they didn't do these ²⁴ well characterized as it is now.

Page 182	_	Proceeded information	- 5	steven M. Lagana, M.D.
though they were conservative, they did 3 go on to state that the association is 4 not likely to be due to chance and I 5 agree with that, also. And I think that 6 since then, the additional literature and 7 my own clinical experience have led me to 8 believe that this is not a chance 9 association, but a causative association. 11 (Deposition Exhibit No. 12 Lagana-9, 2016 Editorial 13 "Sprue-Like Enteropathy Associated 14 With Olmesartan: A New Kid on the 15 Enteropathy Block' by Hujoel and 16 Rubio-Tapia, was marked for 17 identification.) 18 Use MR. PARKER: 19 Q. Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the 25 first listed author? 26 MR. PARKER: Actually, it's 27 the third page of this report 3 A. Third page page 63? 4 A. Third page page 63? 4 A. Okay. 5 A. Okay. 6 Q do you see the box 6 this appears to be well, at the bottom 9 of figure 1, it says, "Proposed 9 management for patients with sprue-like 12 A. Uh-hum. 12 Q. That would be yes, Doctor? 14 A. Uh-hum. 15 Q. That would be yes, Doctor? 16 A. Dh-hum. 17 Q. A proposed algorithm. And 18 A proposed algorithm. And 19 A proposed algorithm. And 20 that was my next question: This is now 21016, four years after the report we just got done looking at. Do you agree with the box that's labeled supporting 24 evidence for this syndrome? 25 MR. PARKER: First listed 26 author. 7 MR. PARKER: First listed 27 A. Uh-hum. 28 The would be yes, Doctor? 29 A. A proposed algorithm. And 29 that was my next question: This is now 29 to the with any all the box that's labeled supporting 20 (and one looking at. Do you agree with 21 to the third page - page 63? 20 A. Okay. 21 A. Uh-hum. 22 to the third page of this rapper - page 63? 24 A. Uh-hum. 25 Q. First listed author? 26 A. Okay. 27 A. Okay. 28 A. A proposed algorithm. 29 A. A proposed algorithm. 29 A. A proposed algorithm. 29 A. Proposed algorithm. 29 A. A proposed algorithm. 29 A. A pro	0.00	5년 경우의 기계 시		
3 go on to state that the association is 4 not likely to be due to chance and I 5 agree with that, also. And I think that 6 since then, the additional literature and 7 my own clinical experience have led me to 6 believe that this is not a chance 9 association, but a causative association. 1	1	And I would go on that even	1	
4 not likely to be due to chance and I 5 agree with that, also. And I think that 6 since then, the additional literature and 7 my own clinical experience have led me to 8 believe that this is not a chance 9 association, but a causative association. 10 11 (Deposition Exhibit No. 12 Lagana-9, 2016 Editorial 13 "Sprue-Like Enteropathy Associated 14 With Olmesartan: A New Kid on the 15 Enteropathy Block" by Hujoel and 16 Rubio-Tapia, was marked for 17 identification.) 18 BY MR. PARKER: 19 BY MR. PARKER: 20 Q. Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the Page 183 2 first listed author? 2 MR. PARKER: Actually, it's 3 the second listed author, was the 4 lead author of the 2012 paper. 4 MR. PARKER: First listed 5 author. 9 MR. SLATER: First listed 6 author. 9 MR. PARKER: 10 Somewhat ambiguous to me. 11 MR. PARKER: 12 You can answer. 13 MR. PARKER: 14 WITNESS: Well, I would 15 Control of the Siral paper. 16 A. Oh, yes. Sorry. 17 Q. Okay. 18 A. Uh-hum. 19 Q. That would be yes, Doctor? 16 A. Oh, yes. Sorry. 17 Q. Okay. 18 A. Oh, yes. Sorry. 19 A. Proposed algorithm. And 20 U. A proposed algorithm. And 21 Under the report we just 22 got done looking at. Do you agree with 22 got done looking at. Do you agree with 23 the box that's labeled supporting 24 evidence for this syndrome? Page 185 MR. SLATER: First listed author. 2 MR. PARKER: 3 the second listed author, was the 1 lead author of the 2012 paper. 3 MR. SLATER: First listed author. 4 WR. PARKER: 5 MR. PARKER: 6 A. Oh, yes. Sorry. 19 A. Okay. 20 Detor, are you familiar 21 You can answer. 22 You can answer. 23 THE WITNESS: Well, I would certainly agree that all of these are potential supportiny pieces of a repotential supportiny pieces of a	2		2	to the third page of this report
4 not likely to be due to chance and I 5 agree with that, also. And I think that 6 since then, the additional literature and 7 my own clinical experience have led me to 8 believe that this is not a chance 9 association, but a causative association. 10	3	go on to state that the association is	3	A. Third page page 63?
6 since then, the additional literature and 7 my own clinical experience have led me to 8 believe that this is not a chance 9 association, but a causative association. 10 11 (Deposition Exhibit No. 12 Lagana-9, 2016 Editorial 13 "Sprue-Like Enteropathy Associated 14 With Olmesartan: A New Kid on the 15 Enteropathy Block" by Hujoel and 16 Rubio-Tapia, was marked for 17 identification.) 18 BY MR. PARKER: 19 BY MR. PARKER: 20 Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the 25 Ifirst listed author? 26 MR. SLATER: First listed 27 author. 38 MR. SLATER: First listed 48 author. 49 MR. PARKER: 40 Q. Doctor, are you familiar 40 with this paper? 5 MR. PARKER: 5 somewhat ambiguous to me. 5 MR. PARKER: 6 author. 7 MR. PARKER: 8 og. Doctor, are you familiar 8 with this paper? A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. And I don't see it in your 28 upplemental reliance list either. A. Al. Uh-hum. 12 Q. Can I call this an 13 algorithm? 14 A. Uh-hum. 15 Q. That would be yes, Doctor? 16 A. Oh, yes. Sorry. 17 Q. Okay. 18 A. A proposed algorithm. 19 Q. A proposed algorithm. 19 Q. A proposed algorithm. 10 A. Oh, yes. Sorry. 10 A. Oh, yes. Sorry. 11 A. Uh-hum. 12 Q. Charl call this an 13 algorithm? 14 A. Uh-hum. 15 Q. That would be yes, Doctor? 16 A. Oh, yes. Sorry. 17 Q. Okay. 18 A. A proposed algorithm. And that was my next question: This is now 19 Q. A proposed algorithm. 19 Q. A proposed algorithm. 19 Q. A proposed algorithm. 10 A. Oh, yes. Sorry. 11 A. Uh-hum. 12 Q. Can I call this an 13 algorithm? 14 A. Uh-hum. 15 Q. That would be yes, Doctor? 16 A. Oh, yes. Sorry. 17 Q. Okay. 18 A. A proposed algorithm. 19 Q. A proposed algorithm. 19 Q. A proposed algorithm. 19 Q. A proposed algorithm. 10 A. Oh, yes. Sorry. 11 A. Uh-hum. 12 don't agree that life the better and the deal proposed algorithm. 12 Go Chay. 13 A Okay. 14 A. Uh-hum. 15 A. Oh, yes. Sorry. 16 A. A Proposed algorithm. 18	4	not likely to be due to chance and I	4	
7 this appears to be well, at the bottom 8 believe that this is not a chance 9 association, but a causative association. 10	5	agree with that, also. And I think that	5	A. Okay.
believe that this is not a chance sasociation, but a causative association. Cheposition Exhibit No. Lagana-9, 2016 Editorial Cheposition Exhibit No. Cheposition Packet Packet No. Opens A Doposed Igorithm. A Uh-hum. Cheposition Packet No. Opens A Doposed Igorithm And Cheposition Salporithm	6	since then, the additional literature and	6	Q do you see the box
be believe that this is not a chance association, but a causative association. Cheposition Exhibit No. Lagana-9, 2016 Editorial Cheposition Exhibit No. Cheposition Packet on the packet of the packet No. Cheposition Stop of the Stop on the First No. Cheposition Stop of the Stop on the Stop	7	my own clinical experience have led me to	7	this appears to be well, at the bottom
9 management for patients with sprue-like enteropathy associated with olmesartan"? 10	8	believe that this is not a chance	8	
10 12 12 13 13 13 14 15 15 15 15 15 15 15	9	association, but a causative association.	9	[[[[[[[[[[[[[[[[[[[
11 (Deposition Exhibit No. Lagana-9, 2016 Editorial 12 20. Can I call this an 13 algorithm? 14 With Olmesartan: A New Kid on the 15 Enteropathy Block" by Hujoel and 16 Rubio-Tapia, was marked for 16 Rubio-Tapia, was marked for 17 identification.) 17 Q. Okay. 18 A. A proposed algorithm. 19 BY MR. PARKER: 19 Q. A proposed algorithm. And 20 Q. Let me move on to Exhibit 20 Q. Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 21 ada author of the 2012 paper. 24 MR. SLATER: You mean the 21 MR. SLATER: You mean the 22 got done looking at. Do you agree with 21 4 MR. SLATER: Objection. 23 THE WITNESS: Well, I would 24 with mis paper? 25 MR. SLATER: First listed author. 3 MR. SLATER: First listed author. 4 with this paper? 3 Q. On the bottom of the first 4 with this paper? 3 Q. On the bottom of diagnosis 3 Q. On the bottom of diagnosis 3 Q. On the bottom of diagnosis 3 A. Okay.	10		10	
"Sprue-Like Enteropathy Associated With Olmesartan: A New Kid on the Enteropathy Block" by Hujoel and Rubio-Tapia, was marked for identification.) 15	11	(Deposition Exhibit No.	11	
"Sprue-Like Enteropathy Associated With Olmesartan: A New Kid on the Enteropathy Block" by Hujoel and Rubio-Tapia, was marked for identification.) 15	12	Lagana-9, 2016 Editorial	12	Q. Can I call this an
With Olmesartan: A New Kid on the Enteropathy Block" by Hujoel and Enteropathy Block" by Hujoel and 15	13	20-3 197 7 - 173 197 - 173 7 970 174 175 175 175 175 175 175 175 175 175 175	13	The state of the s
16 Rubio-Tapia, was marked for identification.) 17 Q. Okay. 18 YMR. PARKER: 29 Q. Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the Page 183 1 first listed author? 2 MR. PARKER: Actually, it's 3 the second listed author, was the 4 lead author of the 2012 paper. 5 MR. SLATER: First listed 6 author. 7 MR. PARKER: First listed 8 author. 9 MR. SLATER: "Lead" is 9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. Okay. 18 A. A proposed algorithm. 19 Q. A proposed algorithm. 10 A. A proposed algorithm. 10 A. A proposed algorithm. 11 A oby yes story. 12 got done looking at. Do you agree with 13 the box that's labeled supporting 14 evidence for this syndrome? 15 MR. SLATER: Objection. 16 You can answer. 17 You can answer. 18 THE WITNESS: Well, I would 19 cerially agree that all of these 19 are potential supportive pieces of 19 evidence. I would not necessarily 10 say that every one of these is 11 page of this paper. 12 A. Okay. 13 Q. On the bottom of the first 14 on the left side of the page, they 15 write, "Confirmation of diagnosis 16 requires clinical resolution of symptoms 17 A. Okay. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 don't agree with that, because I think 22 don't agree with that, because I think 23 treet, 20 Have you published papers in 24 don't agree with that after you stop	14		14	
Rubio-Tapia, was marked for identification.) 16	15	Enteropathy Block" by Hujoel and	15	
17 Identification. 18	16		16	
18	17		17	2.5 C. (C. (C. (C. (C. (C. (C. (C. (C. (C.
19 BY MR. PARKER: 20 Q. Let me move on to Exhibit 21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the Page 183 1 first listed author? 2 MR. PARKER: Actually, it's 3 the second listed author, was the 4 lead author of the 2012 paper. 5 MR. SLATER: First listed 6 author. 7 MR. PARKER: First listed 8 author. 9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. A proposed algorithm. And 18 that was my next question: This is now 2016, four years after the report we just 20 tdone looking at. Do you agree with 21 the box that's labeled supporting 22 evidence for this syndrome? Page 183 MR. SLATER: Objection. You can answer. 1 HE WITNESS: Well, I would 2 certainly agree that all of these 2 are potential supportive pieces of 2 evidence. I would not necessarily 3 say that every one of these is 3 necessary to make the diagnosis. 8 PMR. PARKER: 10 Q. Please turn to the first 11 page of this paper. 12 A. Okay. 13 Q. On the bottom of the first 14 with this paper? 14 A. Okay. 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 19 A. Okay. 19 A. Okay. 10 Do you agree with that? 19 A. Okay. 10 Do you agree with that, because I think 11 that was my next question: This is now with awas my next questions. 12 page of this paper. 1 A. Okay. 1 Do you agree with that? 1 Do you agree with that, because I think 1 resolution is too strong a statement. 1 Page 183 1 the box that's labeled supporting 2 widence for this syndrome? 1 MR. SLATER: Objection. 1 MR. SLATER: Objection. 1 MR. SLATER: Objection. 1 MR. SLATER: Objection. 2 You can answer. 1 HE WITNESS: Well, I would 1 octation in the first 2 A. Okay. 2 On the bottom of the first 3 Do you agree with that; 1 That, I can assure you. 2	18	14. Namangang ag masik 2012 - 12	18	
Q. Let me move on to Exhibit No. 9, which is the most well, a recent, 2016, paper by, at least, the lead author of the 2012 paper. MR. SLATER: You mean the Page 183 first listed author? MR. PARKER: Actually, it's the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: I see. Okay. MR. PARKER: MR. PARKER: I see. Okay. MR. PARKER: M	19	BY MR. PARKER:	19	
21 No. 9, which is the most well, a 22 recent, 2016, paper by, at least, the 23 lead author of the 2012 paper. 24 MR. SLATER: You mean the Page 183 1 first listed author? 2 MR. PARKER: Actually, it's 3 the second listed author, was the 4 lead author of the 2012 paper. 5 MR. SLATER: First listed 6 author. 7 MR. PARKER: First listed 6 author. 9 MR. SLATER: "Lead" is 8 author. 9 MR. SLATER: "Lead" is 9 MR. PARKER: I see. Okay. 11 MR. PARKER: 12 Q. Doctor, are you familiar 4 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 the box that's labeled supporting evidence for this syndrome? 24 which is paper and the box that's labeled supporting evidence for this syndrome? 24 with syndrome? 25 MR. SLATER: Objection. 26 You can answer. 27 THE WITNESS: Well, I would certainly agree that all of these are potential supportive pieces of evidence. I would not necessarily say that every one of these is necessary to make the diagnosis. 28 BY MR. PARKER: 29 Q. Please turn to the first and one the effist are on the left side of the page, they write, "Confirmation of diagnosis after olmesartan withdrawal." 21 Do you agree with that? 22 Q. And I don't see it in your 23 don't agree mith that, because I think resolution is too strong a statement. 24 Q. Have you published papers in which you state that after you stop	20	 Let me move on to Exhibit 	20	10a
recent, 2016, paper by, at least, the lead author of the 2012 paper. MR. SLATER: You mean the Page 183 first listed author? MR. PARKER: Actually, it's lead author of the 2012 paper. MR. SLATER: Objection. You can answer. THE WITNESS: Well, I would certainly agree that all of these author. MR. PARKER: First listed author. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: I see. Okay. MR. PARKER: A. It doesn't ring an immediate bell. Is it in my reliance list? Q. And I don't see it in your supplemental reliance list either. A. Okay. It doesn't look a familiar yagot done looking at. Do you agree with the box that's labeled supporting evidence for this syndrome? MR. SLATER: Objection. You can answer. THE WITNESS: Well, I would certainly agree that all of these evidence. I would not necessarily say that every one of these is necessary to make the diagnosis. BY MR. PARKER: Q. Please turn to the first page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? Do you agree with that? A. Okay. It hink resolution is I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop	21	[19 국가 :	21	
23 lead author of the 2012 paper. 24 MR. SLATER: You mean the	22	이번 2014년에는 그 마시 (1) - 201시 시계시간에 하면 1 Tel (1)에 시간에 201는 이 사고 있는 이번 전에 가르면 다른 12 만나는 그 나는 이 사이트 경기를 하였다고	22	
Page 183 In first listed author? MR. PARKER: Actually, it's the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: Isee. Okay. MR. PARKER: Isee. Okay. MR. PARKER: Isee. Okay. MR. PARKER: Isee. Okay. MR. PARKER: MR. PA	23		23	
first listed author? MR. PARKER: Actually, it's the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: Isea Okay. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: Isee. Okay. MR. PARKER: Outer on the left side of the page, they with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? A. Okay. Q. It is not in your report. That, I can assure you. MR. SLATER: Objection. You can answer. THE WITNESS: Well, I would certainly agree that all of these are potential supportive pieces of evidence. I would not necessarily say that every one of these is necessary to make the diagnosis. BY MR. PARKER: Q. Please turn to the first page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop	24	[40] 20 [40] [40] [40] [40] [40] [40] [40] [40	24	
first listed author? MR. PARKER: Actually, it's the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. PARKER: First listed author. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: I see. Okay. MR. PARKER: D. Please turn to the first page of this paper. A. Okay. Q. On the bottom of the first — on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. Okay. MR. PARKER: A. Okay. MR. PARKER: A. Okay. MR. PARKER: A. Okay. MR. PARKER: Do you agree with that? A. Okay. MR. PARKER: MR. PARKER	_	THE THEORY MANAGEMENT CONTRACTOR OF THE THEORY OF THE THE THEORY OF THE THE THEORY OF THE THE THEORY OF THE THE THE THEORY OF THE THEORY OF THE THEORY OF THE THEORY OF THE		<u> </u>
MR. PARKER: Actually, it's the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. PARKER: First listed author. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: I see. Okay. MR. PARKER: A. Okay. MR. PARKER: D. Please turn to the first page of this paper. A. Okay. MR. Okay. MR. PARKER: Do nothe bottom of the first — on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. Okay. A. I think resolution is — I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop	1		1	(AC) (AE)
the second listed author, was the lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. PARKER: First listed author. MR. SLATER: "Lead" is author. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: I see. Okay. MR. PARKER: I see. Okay. MR. PARKER: Do On the bottom			(2)-1 3-40	2020
lead author of the 2012 paper. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. PARKER: First listed author. MR. SLATER: First listed author. MR. PARKER: First listed author. MR. PARKER: First listed author. MR. SLATER: "Lead" is author. MR. SLATER: "Lead" is author. MR. PARKER: Isee. Okay. MR. PARKER: I see. Okay. MR. PARKER: I see. Okay. MR. PARKER: MR. PARKER: MR. PARKER: I see. Okay. MR. PARKER: MR. PAR			1 30	in the second se
5 MR. SLATER: First listed 6 author. 7 MR. PARKER: First listed 8 author. 9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 A. Okay. 22 Q. And I don't see it in your 23 familiar. 24 MR. SLATER: First listed 5 are potential supportive pieces of 6 evidence. I would not necessarily 7 say that every one of these is 8 necessary to make the diagnosis. 9 BY MR. PARKER: 10 Q. Please turn to the first 10 page of this paper. 11 Page of this paper. 12 A. Okay. 13 Q. On the bottom of the first 14 on the left side of the page, they 15 write, "Confirmation of diagnosis 16 requires clinical resolution of symptoms 17 after olmesartan withdrawal." 18 Do you agree with that? 19 A. I think resolution is I 20 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	1,750,1			
6 author. 7 MR. PARKER: First listed 8 author. 9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 Supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 6 evidence. I would not necessarily 28 say that every one of these is 29 necessary to make the diagnosis. 8 necessary to make the diagnosis. 9 BY MR. PARKER: 10 Q. Please turn to the first 11 page of this paper. 12 A. Okay. 13 Q. On the bottom of the first 14 on the left side of the page, they 15 write, "Confirmation of diagnosis requires clinical resolution of symptoms 16 after olmesartan withdrawal." 17 Do you agree with that? 18 A. I think resolution is I 29 don't agree with that, because I think resolution is too strong a statement. 20 Q. Have you published papers in 21 which you state that after you stop	2015	TO CHI MAD HOUSE	33	
MR. PARKER: First listed author. MR. SLATER: "Lead" is somewhat ambiguous to me. MR. PARKER: I see. Okay. MR. PARKER:			287	A - 프라트 미
8 necessary to make the diagnosis. 9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 19 A. Okay. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 8 necessary to make the diagnosis. 9 BY MR. PARKER: 10 Q. Please turn to the first 11 page of this paper. 12 A. Okay. 13 Q. On the bottom of the first 14 on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." 16 Do you agree with that? 17 A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. 21 Q. Have you published papers in which you state that after you stop				[25] 20, 10, 10, 10, 10, 10, 10, 10, 10, 10, 1
9 MR. SLATER: "Lead" is 10 somewhat ambiguous to me. 11 MR. PARKER: I see. Okay. 12 BY MR. PARKER: 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. 23 familiar. 29 BY MR. PARKER: 20 Q. Please turn to the first 21 page of this paper. 21 A. Okay. 22 A. Okay. 23 Q. On the bottom of the first 24 on the left side of the page, they 25 write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." 26 Do you agree with that? 27 A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. 28 Q. Have you published papers in 29 Wich you state that after you stop	100		V 8	
somewhat ambiguous to me. MR. PARKER: I see. Okay. BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your A. Okay. Q. And I don't see it in your and the first of the page of this paper. A. Okay. Do not the bottom of the first of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. Okay. A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. A. Okay. It doesn't look	3.0		027	
MR. PARKER: I see. Okay. 11 MR. PARKER: 12 A. Okay. 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 10 Q. And I don't see it in your 20 Q. And I don't see it in your 21 Supplemental reliance list either. 22 A. Okay. 23 familiar. 14 A. Okay. 15 Do you agree with that? 26 A. I think resolution is I 27 don't agree with that, because I think 28 Trease turn to the first 29 page of this paper. 20 Q. On the bottom of the first 21 on the left side of the page, they 22 write, "Confirmation of diagnosis 23 after olmesartan withdrawal." 24 Do you agree with that? 25 A. I think resolution is I 26 don't agree with that, because I think 27 resolution is too strong a statement. 28 Q. Have you published papers in 29 Which you state that after you stop				
BY MR. PARKER: 12 A. Okay. 13 Q. Doctor, are you familiar 14 with this paper? 15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 22 A. Okay. 23 A. Okay. 24 A. Okay. 25 A. Okay. 26 A. Okay. 27 A. Okay. 28 A. Okay. 29 A. Okay. 20 A. I think resolution is I 20 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	18.5	somewhat ambiguous to me.	1	
Q. Doctor, are you familiar Q. Doctor, are you familiar Q. On the bottom of the first — on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms from the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." A. Okay. Jo you agree with that? A. I think resolution is — I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop	1 1 1	MP DADVED, Less Olsey	1.1	7 200 8
with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. A. Okay. It doesn't look A. Okay. It doesn't look A. Okay by the bottom of the list write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop	50.000000			page of this paper.
15 A. It doesn't ring an immediate 16 bell. Is it in my reliance list? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 25 write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." 26 Do you agree with that? 27 A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. 25 Q. Have you published papers in which you state that after you stop	12	BY MR. PARKER:	12	page of this paper. A. Okay.
bell. Is it in my reliance list? 16 Do you agree with that? 17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 24 Wite, Command of diagnosis 25 requires clinical resolution of symptoms 26 after olmesartan withdrawal." 28 Do you agree with that? 29 A. I think resolution is I 20 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	12 13	BY MR. PARKER: Q. Doctor, are you familiar	12 13	page of this paper. A. Okay. Q. On the bottom of the first
17 Q. It is not in your report. 18 That, I can assure you. 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 26 It is not in your report. 27 after olmesartan withdrawal." 28 Do you agree with that? 29 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	12 13 14	BY MR. PARKER: Q. Doctor, are you familiar with this paper?	12 13 14	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they
That, I can assure you. 18 Do you agree with that? 19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 28 Do you agree with that? 20 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	12 13 14 15	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate	12 13 14 15	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis
19 A. Okay. 20 Q. And I don't see it in your 21 supplemental reliance list either. 22 A. Okay. It doesn't look 23 familiar. 29 A. I think resolution is I 20 don't agree with that, because I think 21 resolution is too strong a statement. 22 Q. Have you published papers in 23 which you state that after you stop	12 13 14 15 16	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list?	12 13 14 15 16	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms
Q. And I don't see it in your supplemental reliance list either. A. Okay. It doesn't look and I don't see it in your contact in think resolution is a property of think resolution in the property of think resolution is a property of think resolution in the property of think resolution is a property of think resolution in the property of think resolution is a property of the	12 13 14 15 16 17	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report.	12 13 14 15 16	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal."
 supplemental reliance list either. A. Okay. It doesn't look familiar. resolution is too strong a statement. Q. Have you published papers in which you state that after you stop 	12 13 14 15 16 17	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you.	12 13 14 15 16 17	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that?
22 A. Okay. It doesn't look 23 familiar. 22 Q. Have you published papers in 23 which you state that after you stop	12 13 14 15 16 17 18	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay.	12 13 14 15 16 17 18	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I
²³ familiar. ²³ which you state that after you stop	12 13 14 15 16 17 18 19	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your	12 13 14 15 16 17 18 19	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think
L	12 13 14 15 16 17 18 19 20 21	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your supplemental reliance list either.	12 13 14 15 16 17 18 19 20 21	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think resolution is too strong a statement.
2. Okay. Well, then, the just a comesarian, you have resolution of	12 13 14 15 16 17 18 19 20 21 22	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your supplemental reliance list either. A. Okay. It doesn't look	12 13 14 15 16 17 18 19 20 21 22	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in
	12 13 14 15 16 17 18 19 20 21 22 23	BY MR. PARKER: Q. Doctor, are you familiar with this paper? A. It doesn't ring an immediate bell. Is it in my reliance list? Q. It is not in your report. That, I can assure you. A. Okay. Q. And I don't see it in your supplemental reliance list either. A. Okay. It doesn't look familiar.	12 13 14 15 16 17 18 19 20 21 22 23	page of this paper. A. Okay. Q. On the bottom of the first on the left side of the page, they write, "Confirmation of diagnosis requires clinical resolution of symptoms after olmesartan withdrawal." Do you agree with that? A. I think resolution is I don't agree with that, because I think resolution is too strong a statement. Q. Have you published papers in which you state that after you stop

	Proceded information -	100	steven M. Lagana, M.D.
·	Page 186		Page 188
	symptoms?	1	quite specifically on what I ve
2	A. Well, certainly in many	2	seen in the dechallenge biopsies
3	cases, you do. I don't recall if I've	3	and what led me to believe that
4	specifically put that in a paper. I	4	there was a positive dechallenge.
5	might have.	5	How many stools per day
6	Q. So we go back to I'm not	6	difference, that's more of a
7	sure I ever got an answer to my question	7	question for a gastroenterologist,
8	war concurred improvement. If someone	8	I think.
9	has reported diarrhea with ten bowel	9	BY MR. PARKER:
10	movements, or what we see in the papers,	10	Q. Fair enough. In the context
11	Cvactations - 1 love that	11	of your world of pathology, what do you
12	A. Yes.	12	demand to see pathologically in terms of
13	 Q per day and it goes down 	13	improvement, not resolution, but
14	to eight after olmesartan is withdrawn	14	improvement, before you are prepared to
15	and stays at eight, is that sufficient	15	say, this shows dechallenge from the
16	clinical improvement to justify a	16	cessation of olmesartan?
17	diagnosis of sprue-like enteropathy?	17	A. Okay.
18	MR. SLATER: Objection.	18	MR. SLATER: Objection.
19	You can answer.	19	You can answer.
20	THE WITNESS: I think that's	20	THE WITNESS: Okay.
21	too much it's too much of a	21	Assuming that I have a pre an
22	vacuum. You know, you're	22	on-olmesartan biopsy and assuming
23	describing just one factor in a	23	that we're talking about the small
24	patient's care that I would I	24	intestine
<u> </u>			
	Page 187		Page 189
1	Page 187 would really want to know more	1	Page 189 MR. PARKER: We are.
1 2	would really want to know more	1 2	MR. PARKER: We are.
	would really want to know more about the full clinical picture of	55	MR. PARKER: We are. THE WITNESS: Okay then
2	would really want to know more	2	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is
2	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an	2 3	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer
2 3 4	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not.	2 3 4	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before.
2 3 4 5	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER:	2 3 4 5	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less
2 3 4 5 6	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand,	2 3 4 5 6	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina
2 3 4 5 6	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER:	2 3 4 5 6 7	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less
2 3 4 5 6 7 8	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some	2 3 4 5 6 7 8	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less
2 3 4 5 6 7 8	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to	2 3 4 5 6 7 8	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would
2 3 4 5 6 7 8 9	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge.	2 3 4 5 6 7 8 9	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis.
2 3 4 5 6 7 8 9 10	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection.	2 3 4 5 6 7 8 9 10	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer
2 3 4 5 6 7 8 9 10 11	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer.	2 3 4 5 6 7 8 9 10 11	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and
2 3 4 5 6 7 8 9 10 11 12 13	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you	2 3 4 5 6 7 8 9 10 11 12	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less rypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so
2 3 4 5 6 7 8 9 10 11 12 13 14	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there,	2 3 4 5 6 7 8 9 10 11 12 13	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can
2 3 4 5 6 7 8 9 10 11 12 13 14 15	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What	2 3 4 5 6 7 8 9 10 11 12 13 14 15	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement there would really be a	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less rupt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an improvement in one or more of
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement there would really be a determination that a	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less rypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an improvement in one or more of those, I would consider that
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement there would really be a determination that a gastroenterologist would make, not	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an improvement in one or more of those, I would consider that evidence of dechallenge. And the
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement there would really be a determination that a gastroenterologist would make, not a pathologist.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an improvement in one or more of those, I would consider that evidence of dechallenge. And the more improvements that there were,
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	would really want to know more about the full clinical picture of the patient before I said whether two less bowel movements is an improvement or not. BY MR. PARKER: Q. So then help me understand, as a pathologist, what you would expect and demand to determine whether some degree of improvement is enough to constitute dechallenge. MR. SLATER: Objection. You can answer. THE WITNESS: Well, so you used an interesting phrase there, which is as a pathologist. What we're talking about with number of stools per day, the improvement there would really be a determination that a gastroenterologist would make, not	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	MR. PARKER: We are. THE WITNESS: Okay then what I'd like to see is lengthening of the villi, longer villi than what were there before. I would like to see less inflammation, be it in the lamina propria or in the epithelium. I would like to see less subepithelial fibrosis. I would like to see less crypt apoptosis. I would like to see fewer neutrophils and eosinophils and potentially shorter crypts, and so those are most everything that can happen histologically. So I would look at all of those factors and if there was an improvement in one or more of those, I would consider that evidence of dechallenge. And the

Page 190 Page 192 BY MR. PARKER: BY MR. PARKER: Q. Well, maybe that answers my Q. And is normal 40 per 3 next question. I'm not sure. 3 hundred? A. Okay. A. No, that's abnormal. That's Can you quantify terms like what a lot of people use as a threshold 6 -- I wrote down more, less, less. Can for celiac disease, 30 to 40 -you be any more quantitative as to what Q. I thought that was a cut you demand in each of those pathologic line, so I'm wrong about that. findings? A. 20 -- well, different parts 10 A. Yeah, it depends a lot on of the small intestine have different 11 the findings, but we can go through them. cutoffs. In the ileum, which is the most So the villous architecture, a normal distal part of the small intestine, up to 13 villous should be four or five times 40 can be allowed because it's a very 14 immunologically active part of the small ¹⁴ taller than a crypt is deep. 15 So, you know, if -- if at bowel -baseline there's a little tiny nub of a 16 Q. Let's talk about the villous and a big crypt, instead of being 17 duodenum. 18 five times taller, it's one-fifth the 18 A. Yeah, in the duodenum, 20 is size. So I can look at that ratio and generally considered normal, 20 per 100 see is the ratio improving or not. 20 enterocytes. 21 So that's how I would assess 21 Q. So if you had someone who 22 improvement in the architecture of the had 30 lymphocytes in the epithelial 23 villi. tissues and it went down to 25, is that 24 And that's what I'm trying 24 degree of -- of improvement sufficient to Page 191 Page 193 1 to press you on, Doctor. If that 1 to 5 say that's dechallenge? ² ratio goes 1.5 to 5, is that improvement A. Again, these -- these are 3 such that you would say, oh, that's small, difficult to appreciate changes. dechallenge? 4 I would have to look at the whole 5 MR. SLATER: Objection. picture. 6 You can answer. If the villi were a little 7 THE WITNESS: I would say better, if the lymphocytes were a little 8 that that degree of change would 8 less, the lamina propria inflammation was 9 be very difficult for me to a little bit improved, the crypt 10 confidently state is -- on its own apoptotic bodies were a little less 11 is evidence. 11 frequent -- you know, if all of these 12 subtleties -- one of those subtle So in that case then, I 13 would look to other factors like alterations, I don't think I would 14 we -- that we discussed, such as conclude it was a convincing dechallenge. 15 intraepithelial lymphocytosis, so 15 If I had all of them, even 16 I would ask was there 16 if they were just small, subtle 17 intraepithelial lymphocytosis at variations, I would probably suggest that 18 18 the initial presentation and if there had been some clinical improvement. 19 there was, well, I could count how 19 Q. Let's talk about a different 20 many intraepithelial lymphocytes 20 aspect of this. 21 21 there are in the most concentrated A. Sure. 22 areas and then I could compare Q. What is the time course 23 that to the post -- to the -- to 23 after drug cessation that -- beyond which 24 the dechallenge. 24 you would say that can't be attributed to

_	Troccocca informacion		beeven M. Bagana, M.D.
,	Page 194	1.	Page 196
	drug withdrawal?	1	within about six months to a year.
2	A. We're talking about	2	r couldn't really, though, exclude
3	histology now or clinical?	3	any time period.
4	Q. Yes. I'm staying in	4	140W II you had said 25
5	histology.	5	years, would I agree that that's
6	MR. SLATER: Objection.	6	extremely unitkery, I would, but
7	You can answer.	7	
8	THE WITNESS: I think this	8	DI MIC. I MICICLIC.
9	is an area that's still being	9	 Q. So if dechallenge is the
10	investigated, so I am happy to	10	sinequan nom of giving a diagnosis,
11	analogize a little bit to celiac	11	someone would have to wait a year or more
12	disease. In adults with celiac	12	to get a diagnosis.
13	disease, I think several months,	13	MR. SLATER: Objection.
14	three to six months, to see an	14	MR. PARKER: Is that what I
15	appreciable improvement in the	15	understand you to say?
16	histology is fairly normal and	16	
17	there are patients who take about	17	
18	a year. I've seen patients	18	about clinical and histologic
19	improve in three to six months in	19	MR. PARKER: I'm staying on
20	olmesartan enteropathy.	20	histologic, that's correct. For
21	I don't recall seeing	21	그림에 가장되었다면 아이들 그리다 살아가지 않아 가지 아이를 하면 아이들이 아이들이 되었다면 하는데 얼마를 하는데 하는데 하는데 하다니다.
22	patients without any histologic	22	
23	improvement in over a year, but	23	
24	that's I don't recall seeing	24	saying you're not going to
	Page 195		Page 197
1	it. That's not saying it doesn't	1	TOTAL STATE
2	happen.	2	
3	There is in celiac disease	3	[[' [] 2 - 구리 [] 2 - 조리 [] 2 - 그리 []
4	the refractory state, which has	4	MR. SLATER: Objection.
5	not no analogous disease has	5	You can answer.
6	been identified in olmesartan yet,	6	THE WITNESS: No, I don't
7	like refractory olmesartan	7	believe I said that. I think I
8	enteropathy, but it's possible.	8	said that there had to be a
9	BY MR. PARKER:	9	clinical improvement following
10	Q. So going back to my original	10	I didn't put a pathologic
11	question about olmesartan, you said it's	11	improvement as an absolute
12	still being worked out or words to that	12	necessity to make the diagnosis.
13	effect.	13	BY MR. PARKER:
14	A. Uh-hum.	14	Q. Okay. So as long as there's
15	Q. Is there currently no	15	clinical improvement, even though there's
16	outside time limit that after which	16	no pathologic improvement, you're okay
17	you will reject the notion of there being	17	with doctors putting the diagnosis of
18	dechallenge?	18	sprue-like enteropathy on someone;
19	MR. SLATER: Objection.	19	correct?
20	You can answer.	20	A. If there's clinical
21	THE WITNESS: Well, I think	21	improvement, but there's no pathologic
22	that I would say that most	22	improvement, you're saying.
23	patients who have been biopsied	23	Q. Yes, sir.
24	post dechallenge have improved	24	A. I would consider it an
	Lan are manage mate unbrotten		and a mount outsider it all

	Protected Information -	٠ ٤	steven M. Lagana, M.D.
- 21	Page 198		Page 200
	exceptional case and I would consider it,	1	You can answer.
2	nom my end, the diagnosis to be somewhat	2	THE WITNESS: If the drug is
3	ancertain. But I would not II an	3	still within someone's so
4	experienced gastroenterologist thought	4	there's been no dechallenge.
5	that was the diagnosis and I had no	5	MR. PARKER: No, let me
6	better diagnosis, I wouldn't fight with	6	start again. My question wasn't
7	him on it.	7	clear.
8	 Q. And, Doctor, is it within 	8	BY MR. PARKER:
9	your area of expertise if not, I'll	9	 You understand the concept,
10	move on to discuss now with me what	10	
11	degree of clinical improvement would be	11	A. I do.
12	needed before someone can conclude	12	Q. Do you know the half-life of
13	there's been successful dechallenge?	13	olmesartan?
14	MR. SLATER: Objection.	14	A. I believe it's about 13
15	You can answer.	15	hours.
16	MR. PARKER: In the context	16	Q. And do you know how many
17	of sprue-like enteropathy,	17	days would have to elapse before all the
18	THE WITNESS: I think it's a	18	metabolites or the parent compound were
19	better question for a	19	out of one's body?
20	gastroenterologist.	20	A. There's a calculation that
21	BY MR. PARKER:	21	can be done. I haven't done it.
22	Q. Let's turn now to	22	Q. It would be a number of
23	rechallenge. Doctor, is there a period	23	days, we can agree upon that
24		24	A. I would.
	Page 199		60 000/0
1	baseline before they're rechallenged to	1	Q if 13 hours is the
2	any type of a drug before you can say	2	half-life? Okay. And what you're
3	- 16일 기원 기계(17일)		telling me, Doctor, is, if you resumed
4	MR. SLATER: Objection.	4	olmesartan within the period of time in
5	You can answer.	5	which half-life has not expired with
6	THE WITNESS: Return to		me so far?
7	baseline meaning their normal	7	A. Yes.
8	state of health?	8	Q. Okay and symptoms
9	MR. PARKER: Normal state of	9	resumed, you would say that that's a
10	health, yes, sir.	10	successful rechallenge?
11	THE WITNESS: I don't think	11	MR. SLATER: Objection.
12	that you need to require anyone to	12	You can answer.
13	return to their normal state of	13	THE WITNESS: That's a
14	health before you can say that	14	pretty vague question. It could
15	there's been a successful	15	encompass a lot of clinical
16	dechallenge.	16	scenarios. If a patient stopped
17	BY MR. PARKER:	17	olmesartan for several days, was
18	Q. So if a drug, any drug, is	18	feeling better, having a clinical
19	suspected of causing an enteropathy and	19	
20	while it is still in someone's system and	20	response, and then restarted
21	you restart that drug and that person has	21	olmesartan and immediately felt
22	symptoms again, you would call that a	22	worse, I could accept that as a
23	successful rechallenge?		dechallenge/rechallenge. BY MR. PARKER:
24	MR. SLATER: Objection.	24	Q. So going back to my example
	MIN. SEATER, OUICUIOII.	= 7	O. BURUME DACK TO MY EXAMPLE
	व्यक्ष्यक्रमा । स्वताक्रमा । स्वताक्ष्यमा । स्वताक्ष्यमा । स्वताक्ष्यम् । । स्वताक्ष्यम् । । स्वताक्ष्यम् । स्	177.2	Qr as gamg sum is my mampio

/	FIOCECCEG IIIIOIMACION -		steven M. Bagana, M.D.
120	Page 202	- 44	Page 204
	and if you're not comfortable because		there's variability in the world, Doctor,
10.10	we're dealing with clinics, then you	2	what is the expected period of time in
3	clinical questions if someone comes in	3	which you would expect to see clinical
4	and says, Doc, you know, I got ten bowel	4	improvement.
5	movements a day, I got this terrible	5	MR. SEATER. Objection.
6	diarrhea, I've had it for a number of	6	You can answer.
7	days, and the doctor says stop your	7	THE WITNESS: Clinical
8	olmesartan. After three days, it goes	8	improvement, not histological
9	down to seven bowel movements. Patient	9	improvement?
10	goes back on olmesartan, it goes back up	10	MR. PARKER: We're going to
11	to ten, is that in your opinion	11	go clinical first.
12	successful dechallenge and rechallenge?	12	THE WITNESS: Weeks.
13	MR. SLATER: Objection	13	MR. PARKER: Weeks. Okay.
14	again.	14	BY MR. PARKER:
15	You can answer.	15	Q. And if the person has been
16	THE WITNESS: Well, it's	16	on a gluten-free diet then for months
17	really it would be a clinical	17	with no clinical improvement, would you
18	judgment on the part of the	18	say that was a failed dechallenge?
19	gastroenterologist. If you want	19	MR. SLATER: Objection.
20	me to opine on it, I can, but	20	You can answer.
21	MR. PARKER: No. I'm asking	21	THE WITNESS: I would say
22	you to opine on it only if you	22	that it becomes less likely, but I
23	have a considered expert opinion.	23	wouldn't necessarily say it
24	If you're speculating and you want	24	failed. I would want to know more
	Page 203		Page 205
1	to must to a CT thatla manfactle.		about the metions
1	to punt to a GI, that's perfectly	1	about the patient.
2	fine with me, also.	2	about the patient. If they had a negative
1			If they had a negative
2	fine with me, also.	2	
2 3	fine with me, also. THE WITNESS: All right.	2	If they had a negative celiac genotype and they had never
2 3 4	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to	2 3 4	If they had a negative celiac genotype and they had never had celiac antibodies, then I
2 3 4 5	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that.	2 3 4 5	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your
2 3 4 5 6	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer.	2 3 4 5 6	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on.
2 3 4 5 6 7	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to	2 3 4 5 6 7	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise
2 3 4 5 6 7 8	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI.	2 3 4 5 6 7 8	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or
2 3 4 5 6 7 8	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right.	2 3 4 5 6 7 8	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I
2 3 4 5 6 7 8 9	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else.	2 3 4 5 6 7 8 9	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my
2 3 4 5 6 7 8 9 10 11	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER:	2 3 4 5 6 7 8 9 10	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be
2 3 4 5 6 7 8 9 10 11	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue	2 3 4 5 6 7 8 9 10 11	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I
2 3 4 5 6 7 8 9 10 11 12 13	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different	2 3 4 5 6 7 8 9 10 11 12	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the
2 3 4 5 6 7 8 9 10 11 12 13	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten.	2 3 4 5 6 7 8 9 10 11 12 13 14	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed.
2 3 4 5 6 7 8 9 10 11 12 13 14	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay.	2 3 4 5 6 7 8 9 10 11 12 13 14	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER:
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me and I'll move on.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology. A. Okay.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me and I'll move on. A. Sure.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology. A. Okay. Q. In a patient with a
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me and I'll move on. A. Sure. Q. When someone who is worked	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology. A. Okay. Q. In a patient with a diagnosis of celiac disease who goes on a
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me and I'll move on. A. Sure. Q. When someone who is worked up and is thought by clinicians and	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology. A. Okay. Q. In a patient with a diagnosis of celiac disease who goes on a gluten-free diet, what's the time course
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	fine with me, also. THE WITNESS: All right. MR. SLATER: Objection to the whole entire lead-in on that. You can answer. THE WITNESS: I'm happy to punt that to a GI. MR. PARKER: All right. Good. We'll talk to someone else. BY MR. PARKER: Q. Doctor, I want to pursue this discussion, but using a different substrate, gluten. A. Okay. Q. Again, as always, if this is outside your area of expertise, tell me and I'll move on. A. Sure. Q. When someone who is worked up and is thought by clinicians and pathologists such as yourself to have	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	If they had a negative celiac genotype and they had never had celiac antibodies, then I would say you're wasting your time, move on. If the patient had otherwise fairly typical symptoms of or presentation of celiac disease, I would not be and I was asked my opinion, because I would not be the one making this decision, I would not be satisfied that the gluten dechallenge had failed. BY MR. PARKER: Q. Let's turn to histopathology. A. Okay. Q. In a patient with a diagnosis of celiac disease who goes on a gluten-free diet, what's the time course when one is on a gluten-free diet that

	or Protected Information '-	- 2	steven M. Lagana, M.D.
	Page 206	Ĭ	Page 208
1	MR. SLATER: Objection.	1	keep my word, whenever you want a
2	You can answer.	2	그렇게 되었다면서 하나 그리고 그리고 그리고 그리고 그리고 있다면 하는데 하는데 그리고
3	THE WITNESS: Months would	3	State of the control
4		4	
5		5	
6		6	
7	mean, I wouldn't necessarily expect any	7	"다"이 등이용하다 (17일 사용 등이라고 기타를 보면 1일 시간 등이 되었다고 있다면 보다 (1일 시간 기타를 보면 12일 시간 기타를 보면 12일 시간 기타를 보면 12일 시간 기타를 보면 12
8	improvement until months have gone by	8	. CISSIA DE LA DA CARLA DE LA CONTRA DEL CONTRA DE LA CONTRA DEL CONTRA DE LA CONTRA DEL CONTRA DE LA CONTRA DE LA CONTRA DEL CONTRA DE LA CONTRA DEL CONTRA DE LA CONTRA DE L
9	A. Right.	9	right odck.
10	Q on the diet?	10	174 의 전에 없이라면 하게 되었다. 이 성의 1일 하는 기계를 되어 생생하게 보다 하지 않아 생생하다.
11	A. Right. I wouldn't not	11	2.27 p.m. to 2.40 p.m.)
12	that you can't see it. You can see it,	12	
13	but I wouldn't necessarily expect it	13	
14	until a few months had passed.	14	
15	Q. Are you familiar with	15	this point.
16	randomized clinical trials referred to as	16	A. I do.
17	N-of-1 trials?	17	[10] [10] [10] [10] [10] [10] [10] [10]
18	A. Randomized clinical trial	18	Q. 140W, Without repeating, out
19	I've heard of N-of-1. I'm not sure I	19	just setting the framework for my next
20	understand N-of-1 in the context of an	20	series of questions, Doctor, if I recall
35.55	RCT.	21	our discussion earlier, at the time Mr.
22	Q. In terms of let me are	22	States asked you to write this report,
23	you familiar with the method of doing a	23	you had already formed your opinion on
24	clinical trial in one patient where that		general causation for the reasons that you described earlier.
THE COT.	chinear trial in one patient where that	A	you described earlier.
			■ 18m 564 4535 - 454 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
	Page 207		Page 209
1		1	The Control of the Co
1 2	Page 207		Page 209 A. I had formed the bulk of my
1 2 3	Page 207 patient is blinded and the physician is		Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater.
2	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or	1 2	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay.
2	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo?	1 2 3 4	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make
2 3 4 5	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At	1 2 3 4 5	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I
2 3 4 5	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program	1 2 3 4 5	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere,
2 3 4 5 6	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At	1 2 3 4 5	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4,
2 3 4 5 6 7	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal	1 2 3 4 5 6 7	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere,
2 3 4 5 6 7 8	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the	1 2 3 4 5 6 7 8	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8
2 3 4 5 6 7 8	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal	1 2 3 4 5 6 7 8	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay.
2 3 4 5 6 7 8 9	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried.	1 2 3 4 5 6 7 8 9	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to
2 3 4 5 6 7 8 9 10	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means	1 2 3 4 5 6 7 8 9 10	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted
2 3 4 5 6 7 8 9 10 11	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you	1 2 3 4 5 6 7 8 9 10 11	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above.
2 3 4 5 6 7 8 9 10 11 12 13	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means	1 2 3 4 5 6 7 8 9 10 11 12 13	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what
2 3 4 5 6 7 8 9 10 11 12 13	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is	1 2 3 4 5 6 7 8 9 10 11 12 13	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you
2 3 4 5 6 7 8 9 10 11 12 13 14 15	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with.	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on.	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay.	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation?
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay. Q. Let's talk about your	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	Page 209 A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation? A. Well, I think the
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay. Q. Let's talk about your report.	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation? A. Well, I think the scientifically accepted method for any
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-I program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-I certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay. Q. Let's talk about your report.	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation? A. Well, I think the scientifically accepted method for any physician to stay abreast of new
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay. Q. Let's talk about your report. A. Can we do five minutes before we do that?	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation? A. Well, I think the scientifically accepted method for any physician to stay abreast of new developments in medicine is to review the
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	Page 207 patient is blinded and the physician is blinded to whether they're taking drug or placebo? A. I don't think that I'm terribly familiar with that. At Columbia, we do have an N-of-1 program where patients with various cancers can have their tumors implanted in an animal model and the tumors are grown in the animal model and various therapeutics are tried. So N-of-1 certainly means something some neurons fire when you say that, but what you just described is not the situation that I'm totally familiar with. Q. Okay. Then I'll move on. A. Okay. Q. Let's talk about your report. A. Can we do five minutes	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	A. I had formed the bulk of my opinion before I spoke to Mr. Slater. Q. Okay. And, Doctor, you make reference to, in here let me see if I can find it I think it's elsewhere, but I see it in the last section, 4, under opinions, on the last page, page 8 A. Okay. Q you make reference to applying the scientifically accepted methods set forth above. Can you describe for me what methods you have in mind that you discussed in this report by which or through which you reached an opinion on general causation? A. Well, I think the scientifically accepted method for any physician to stay abreast of new

	Protected Information -	i k	steven M. Bagana, M.D.
(4)	Page 210		Page 212
	experiences with various entities, which		that the Marthey paper where they report
2	I've done, to discuss new entities with	2	the results of a survey is an
3	your colleagues and experts, which I've	3	epidemiological study?
4	done, and I would say that those are the	4	A. I'd have to I'd have to
5	scientifically accepted methods which I	5	look at it again. I would be happy to
6	have employed.	6	look at it again if you want to wait.
7	Q. We can agree that in the	7	Q. Well, why don't you take a
8	report itself, there's no discussion of	8	look at your description of the Marthey
9	any of the literature reporting on	9	study on page 7, see if that helps first,
10	epidemiological studies; correct?	10	of your report.
11	 A. Let's double-check. 	11	 Well, I did just read that.
12	Q. Sure.	12	I would agree with you that epidemiology
13	(Pause.)	13	is not an important part of the document
14	THE WITNESS: I believe	14	that I produced, the written document.
15	we can clarify this if necessary	15	Q. And I agree with that I
16	I believe that the Theophile	16	mean, I accept that.
17	article, number 23, and the	17	A. Okay.
18	Marthey article, get into	18	Q. My question is, you're not
19	epidemiology; but the	19	describing Marthey as an epidemiological
20	epidemiologic article that I	20	study, are you?
21	consider most important is the	21	 A. Let me double-check it.
22	Basson article, which I did not	22	Q. Please.
23	reference.	23	(Pause.)
24	MR. PARKER: My question I	24	THE WITNESS: Not in the
	Page 211		Page 213
1	don't believe was did you	1	classic sense. It overlaps with
2	reference anything. My question	2	epidemiology, of course, if you
3	is, did you have a discussion of	3	survey a population of of
4	that in your report.	4	gastroenterologists, but it's not
5	THE WITNESS: Ah, okay. I'm	5	by any means a classic
6	going to take another look.	6	epidemiology study.
7	MR. PARKER: Please.	7	BY MR. PARKER:
8	(Pause.)	8	Q. There are no controls in the
9	THE WITNESS: I would say a	9	study at all; correct?
10	passing reference was made to the	10	A. Correct.
11	question of epidemiology where I	11	Q. And that is one of the
12	on page 7, I talk about how	12	essential tools in epidemiological
13	Marthey, et al conducted a survey	13	research, is it not?
14	of French gastroenterologists and	14	A. It is.
15	discovered 36 cases, which one can	15	Q. Okay.
16	make an inference about the	16	Doctor, do you adhere to the
17	epidemiology of olmesartan	17	practice of evidence-based medicine?
18	enteropathy in France on the basis	18	MR. SLATER: Objection.
19	of that article.	19	You can answer.
20	But I would agree that major	20	THE WITNESS: Of course. I
21	emphasis to epidemiology is not	21	believe everyone does these days.
22	present in my report.	22	BY MR. PARKER:
23	BY MR. PARKER:	23	Q. Some do not, trust me.
1			
24	Q. Are you telling me, sir,	24	A. Fair enough.

	Protected Information -		oceven m. nagana, m.b.
100	Page 214		Page 216
1	Q. Tell me what that phrase	3,	If I would say that
2	means to you, Doctor.	2	before I did some of the reading,
3	 A. Well, evidence-based 	3	such as ROADMAP, Padwal I think
4	medicine means that we base our decision	4	those two in particular they
5	making, our diagnostic algorithms, our	5	make me think that this is
6	treatment algorithms on the basis of the	6	probably a pretty uncommon event
7	published literature and scientific	7	
8	studies and not on, say, you know, expert	8	nonexistent are two very different
9	opinion or things of that sort.	9	things.
10	 Q. Doctor, it is not uncommon 	10	So I am firm that this
11	when scientists publish in the	11	that this association is real and
12	peer-reviewed literature, particularly in	12	causative. I think considering
13	a good journal, that you're required by	13	these two studies, particularly
14	the editors to disclose the limitations	14	ROADMAP, didn't find a real signal
15	of one's study?	15	for enteropathy probably means
16	A. Yeah, I think that's common.	16	that because they that they
17	Q. You said at the outset of	17	were underpowered to detect what I
18	the deposition, you approached this task	18	believe to be an uncommon event.
19	as a scientist would, looking at evidence	19	BY MR. PARKER:
20	on both sides of the issue; correct?	20	Q. I'm waiting I wasn't sure
21	A. Yes.	21	whether you were finished with your
22	Q. Explain for me, as you	22	answer.
23	looked at the evidence in the course of	23	A. That's it.
24	preparing this report, what did you	24	Q. So if I can understand, my
_	Page 215	-	Page 217
1	consider to be the strongest reliable	1	(F)
2	evidence arguing against your position of		question was phrased in terms of what did you find to be the strongest evidence
1 35			
3	deneral concetton/	1920	
3	general causation?	3	that was inconsistent with your opinion,
4	MR. SLATER: Are you going	3 4	that was inconsistent with your opinion, not that it persuaded you, on general
3 4 5	MR. SLATER: Are you going to pay him a fee for that?	3 4 5	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is,
4 5 6	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already	3 4 5 6	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm
4 5 6 7	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him	3 4 5 6 7	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me.
4 5 6 7 8	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you	3 4 5 6 7 8	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection.
4 5 6 7 8 9	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more.	3 4 5 6 7 8	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer.
4 5 6 7 8 9	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a	3 4 5 6 7 8 9	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat
4 5 6 7 8 9 10	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list.	3 4 5 6 7 8 9 10	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted
4 5 6 7 8 9 10 11	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please.	3 4 5 6 7 8 9 10 11	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer?
4 5 6 7 8 9 10 11 12	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time.	3 4 5 6 7 8 9 10 11 12 13	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure.
4 5 6 7 8 9 10 11 12 13 14	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too	3 4 5 6 7 8 9 10 11 12 13	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER:
4 5 6 7 8 9 10 11 12 13 14 15	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding.	3 4 5 6 7 8 9 10 11 12 13 14 15	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to
4 5 6 7 8 9 10 11 12 13 14 15 16	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.)	3 4 5 6 7 8 9 10 11 12 13 14 15 16	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you
4 5 6 7 8 9 10 11 12 13 14 15 16 17	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find
4 5 6 7 8 9 10 11 12 13 14 15 16 17	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me think, maybe this association is	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was inconsistent with your general causation
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me think, maybe this association is spurious, maybe it's not	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was inconsistent with your general causation opinion.
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me think, maybe this association is spurious, maybe it's not causative. I didn't have that	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was inconsistent with your general causation opinion. A. Okay.
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me think, maybe this association is spurious, maybe it's not causative. I didn't have that opinion based on anything that I	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was inconsistent with your general causation opinion. A. Okay. MR. SLATER: Objection;
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	MR. SLATER: Are you going to pay him a fee for that? MR. PARKER: I've already made you well, I've made him money. He's going to bill you some more. THE WITNESS: Give me a minute to look through the list. MR. PARKER: Please, please. Take your time. MR. SLATER: Don't think too hard. No, I'm just kidding. (Pause.) THE WITNESS: Well, I really came across nothing that made me think, maybe this association is spurious, maybe it's not causative. I didn't have that	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	that was inconsistent with your opinion, not that it persuaded you, on general causation; and I think your answer is, Padwal and the ROADMAP study. But if I'm wrong, you correct me. MR. SLATER: Objection. You can answer. THE WITNESS: Can you repeat again the question that you wanted me to answer? MR. PARKER: Sure. BY MR. PARKER: Q. The question I want you to answer is, what evidence, if any, as you reviewed the literature did you find presented the best evidence that was inconsistent with your general causation opinion. A. Okay.

Page 218 Page 220 THE WITNESS: I don't think Q. In an unbiased, scientific 2 anything was really inconsistent sort of a way? 3 with my opinion. A. Yeah. I certainly didn't go 4 into it with bias -- with any cognitive 4 5 (Deposition Exhibit No. biases I was aware of anyway. 6 Lagana-10, 2016 Article Q. I'm asking, was part of your 7 "Olmesartan-associated sprue-like intent in writing this paper to convince 8 enteropathy: a systematic review others that olmesartan was, in fact, 9 with emphasis on histopathology" causing sprue-like enteropathy? 10 by Burbure, Lagana, et al, was 10 A. No, that really -- the 11 marked for identification.) reason why I wanted to write this paper 12 was really to discuss the histologic 13 BY MR. PARKER: differential diagnosis and to talk about 14 Q. Let's turn now to Exhibit the pathology of it. 15 15 No. 10, which is your 2016 paper --Convincing others that this 16 A. Sure. existed was not really a big part of my 17 Q. -- with colleagues. Do you 17 thinking when I was putting this 18 have it, Doctor? together. 19 19 A. I do. Q. Let's go through some of the 20 Q. For the record, this is the things you say in this paper. If we look paper that you published with others. just at the summary -- and I'm going to You are the last author in this paper; 22 say "you," but this was a collaborative correct? effort; correct? 24 24 Correct. A. Yeah. Page 219 Page 221 1 Q. All right. 1 Q. Okay -- were you the primary 2 And I think you describe author? 3 this in your report as one in which you A. Meaning did I write most of 4 were the senior author. what is here? A. Yes. Q. Did you write the -- at least the first draft of this? Q. Certainly not senior to ⁷ Peter Green, but certainly -- well, let A. I wrote a fair amount of ⁸ me ask you, in all seriousness, what does this. I didn't write all of this. It 9 that mean to say that you're the senior would be tough now for me to remember author on this paper? exactly what phrases or paragraphs I 11 wrote and what phrases or paragraphs A. It means that the concept of 12 this particular paper was mine and that I someone else wrote. 13 guided the project from beginning to Q. And I'm not going to ask you ¹⁴ completion. 14 that question, but --15 15 Q. What does it mean -- the Okay. I wrote some of it. A. 16 title of your paper is 16 Q. Okay. And other than "Olmesartan-associated sprue-like yourself, was there one or others of here enteropathy: a systematic review with who were what you would describe as major emphasis on histopathology." contributing authors of the piece? 20 What does it mean to do a 20 A. How would you define major systematic review? 21 contributor? 22 A. Systematic review means that Q. Did some original drafting 23 we attempted to address all the published of certain sections of the paper as 24 literature on this topic in this paper. opposed to simply reviewing and offering

Page 222 Page 224 editorial suggestions. A. To the best of my knowledge, A. Dr. Burbure, who was the we have a couple of patients like that. 3 first author on the paper, did a fair bit Q. And do you know what drugs 4 of the writing. they were on? Q. Anyone else, sir? Other 5 A. I have vague recollections. than yourself obviously. I wouldn't -- I couldn't really swear to A. I would say the two of us them in a court of law. did the vast majority of the -- of the Q. Doctor, what other -- I drafting of verbiage. recall not having asked you this 10 Q. So let's turn then to the question: What other drugs in your 11 summary. You wrote, "It is not well medical training and experience do you 12 established if other ARBs cause such a accept as causes of enteropathy, putting syndrome, although case reports suggest aside ARBs? that it can"; correct? 14 A. Well, one that we see fairly frequently -- well, one that we see A. Yes. 16 O. And we will talk a little occasionally, I should say -- at Columbia ¹⁷ bit later about your discussion of those, is mycophenolate or products derived from 18 but how do the case reports of the A -mycophenolic acid, which is used as an 19 of the other ARBs differ from olmesartan immunosuppressant drug in patients with other than the number of them? organ transplantation. That can 21 21 occasionally cause similar enteropathic A. Sorry. I'm -- one of my 22 friends always says, "If my aunt had ²² changes which could be morphologically 23 similar to what we see with angiotensin different anatomy, she'd be my uncle." But, anyway, the number of 24 receptor blockers. Page 223 Page 225 them happens to be I think a very Other drugs that we see --² important piece here. That's how they ² well, NSAIDs are a common drug. We often 3 differ. There's -see some inflammation of the intestines Q. That's fine. 4 in patients who are NSAID users. A. -- just a couple as compared I would say this particular pattern that -- the patterns that we've 6 to over a hundred. Q. There are no trick questions seen with -- we don't typically see a sprue-like enteropathy in NSAID users, yet. Okay. but it's plausible and probably has come So other than the number, 10 there's no other substantive difference across my desk over the years. 11 in the case reports of other ARBs and Q. Is the variability as you 12 enteropathy versus olmesartan. Are we in 12 have described it today in the agreement? histopathology in patients using 14 A. Of the case reports I've olmesartan replicated with any other drug 15 read of other ARBs causing enteropathy, I that you accept as a cause of enteropathy?

16 would say that they look very similar to 17 olmesartan.

18 Q. And does the group at 19 Columbia have patients who have gone on other ARBs -- "other" meaning 21 non-olmesartan -- and who have developed

²² an enteropathy after which they improved 23 after discontinuation that have not found

²⁴ a way into the peer-reviewed literature?

17 A. Let me just rephrase that back to you and make sure I understood it right. 20 O. Yeah. A. Do other drugs which cause 22 enteropathy have as broad a spectrum as 23 olmesartan? 24 I managed to get the

Page 226 Page 228 1 question out. You managed to understand With regard to the one who 2 it, yes. 2 -- if I'm reading this correctly -- did A. Okay. Good. Yeah. 3 not have improvement in histology, going 4 mycophenolate can have very variable 4 back to our earlier discussion, would you presentation from very, very subtle say that that person still had abnormalities to total villous atrophy, dechallenge? yes. A. Well, so first, this is not Q. So if I were to pull out my work. This is a reference to another ⁹ literature on that drug, I would see -- to another paper and I believe I'm 10 histologic descriptions of it that would referencing Rubio-Tapia there, so let me approximate what you've written in papers see -- yeah, so referencing Rubio-Tapia, 12 such as the one we're talking about now and I believe in the Rubio-Tapia paper --13 regarding olmesartan. 13 I believe they all had improvements, but 14 A. Yeah, you could find such 14 let me just double-check this. 15 descriptions. 15 Q. Sure. 16 16 Q. Let's go on then. On the Α. So they described 17 cases 17 summary, you also wrote -with histologic recovery of the duodenum, 18 A. Summary on page 1, you mean? 17 of 18, and one case with focal partial 19 Q. Yes, sir. villous atrophy, but they don't say what 20 A. Okav. that patient had before, so I couldn't 21 -- there are no guidelines say if there had been some improvement or 22 regarding the histopathologic 22 not in that patient. 23 distinctions of olmesartan-associated 23 Q. Let's go on to numbered page ²⁴ enteropathy from other causes of sprue. 130. You write on the right-hand column Page 227 Page 229 and then you give some parenthetical -- and you're referring back to a couple ² examples; correct? ² cases in the literature -- you write, 3 A. Uh-hum. 3 "These observations are consistent with Q. And we touched upon this a 4 our experience where patients typically 5 little bit earlier in the deposition and 5 start to notice great improvement just you stand by this statement. days after medication cessation." Let me A. I believe so. stop there. Q. Well, only you know, Doctor. Does what you wrote here A. That was the main purpose of describe the majority of your patients? this article, was to help pathologists And when I say "yours," I mean the 11 who may be encountering this entity to patients seen at Columbia? 12 differentiate it from other entities 12 A. I'm sorry. The word you which may histologically resemble 13 used there was great majority? ¹⁴ olmesartan enteropathy. 14 Q. Yeah. So, yeah, there are no 15 A. I couldn't say if it 16 official guidelines anywhere. This is my 16 represents the great majority. It or our best take on it. certainly represents many patients. In 18 Q. Let's go on to the next page fact, that's how Joe Murray discovered 19 then. At the bottom of the left-hand this association in the first place, is 20 column, you write, "Clinical symptoms patients staying in the hospital who 21 resolved quickly after cessation of the weren't on their olmesartan for even a

23 histologic changes disappeared in the

22 medication in all cases and the

24 vast majority (17 of 18)."

22 few days reported to him that they

Q. So I'm not surprised at

23 started feeling better.

24

-	d 020 Protected Information		
152	Page 230		Page 232
1	trial, are you able to say that the	1	it completely accurately, but you
2	majority of the patients seen at Columbia	2	can answer.
3	and a second sec	3	MR. PARKER: Well, I
4	taking olmesartan and are told to stop	4	certainly wanted to, so I'll try
5	taking officesartan have, to use your	5	it one more time.
6	moras, great improvement just days after	6	MR. SLATER: I know what you
7	medication cessation?	7	
8	 A. That would be my 	8	in life. Just making an
9	understanding based on discussions had at	9	
10	emineopathologic conferences,	10	BY MR. PARKER:
11	interdisciplinary conferences.	11	Q. "This broadens the
12	But Dis. Green and Lebwoni	12	differential even further and there is no
13	would be better able to speak to that and	13	cardinal finding which can establish the
14	both reviewed this paper for accuracy, so	14	diagnosis of olmesartan-induced injury
15	10 M	15	based solely on histopathology," does
16	Q. Let's go on to numbered page	16	that remain your opinion today?
17	131 let's go to page 132.	17	A. It does.
18	A. Sure.	18	Q. Under celiac disease,
19	Q. You reference here clinical	19	section 5.1, the last sentence,
20	trials of some of the other ARBs,	20	
21	particularly azilsartan. Do you see	21	are the most meaningful discriminators
22	that?	22	between celiac disease and ARB
23	A. Yep.	23	enteropathy," does that remain your
24	Q. Did you review the clinical	24	opinion today?
1		1	Control of the Contro
	Page 231		Page 222
1	Page 231	1	Page 233
1 2	trials of azilsartan medoxomil for	1 2	A. We should have included
1 2 3	trials of azilsartan medoxomil for purposes of writing this paper?	2	A. We should have included no, I think a response to a dechallenge
2	trials of azilsartan medoxomil for purposes of writing this paper? A. No.	3	A. We should have included no, I think a response to a dechallenge with of ARB is probably more
3	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that?	3	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful.
3	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference	2 3 4 5	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite
2 3 4 5 6	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean?	2 3 4 5 6	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten
2 3 4 5 6 7	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical	2 3 4 5 6 7	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today?
2 3 4 5 6	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan.	2 3 4 5 6 7 8	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say
2 3 4 5 6 7 8	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article	2 3 4 5 6 7 8	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately,
2 3 4 5 6 7 8	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement.	2 3 4 5 6 7 8 9	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement
2 3 4 5 6 7 8 9	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably.	2 3 4 5 6 7 8 9 10	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB
2 3 4 5 6 7 8 9 10	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't.	2 3 4 5 6 7 8 9 10 11	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful
2 3 4 5 6 7 8 9 10 11 12	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then.	2 3 4 5 6 7 8 9 10 11 12 13	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and
2 3 4 5 6 7 8 9 10 11 12 13	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of	2 3 4 5 6 7 8 9 10 11 12 13 14	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy.
2 3 4 5 6 7 8 9 10 11 12	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you	2 3 4 5 6 7 8 9 10 11 12 13 14 15	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on.
2 3 4 5 6 7 8 9 10 11 12 13 14 15	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure,	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence.
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no cardinal finding which can establish the	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence. Q. Earlier just so I'm sure
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no cardinal finding which can establish the diagnosis of olmesartan-induced injury	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence. Q. Earlier just so I'm sure I'm understanding, seronegativity and
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no cardinal finding which can establish the diagnosis of olmesartan-induced injury based on histopathology.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence. Q. Earlier just so I'm sure I'm understanding, seronegativity and lack of response to a gluten diet don't
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no cardinal finding which can establish the diagnosis of olmesartan-induced injury based on histopathology. That remains your view	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence. Q. Earlier just so I'm sure I'm understanding, seronegativity and lack of response to a gluten diet don't rule out celiac disease. Would you
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	trials of azilsartan medoxomil for purposes of writing this paper? A. No. Q. Do you recall who did that? A. Who referenced the reference 28, you mean? Q. Who reviewed the clinical trials of azilsartan. A. You mean who found article 28 and included it in the statement. Q. And studied it, presumably. A. I don't. Q. Okay. Let's go on then. Down at the bottom of section 5, I think this confirms what you said earlier, but let me just make sure, you wrote: This broadens the differential even further and there is no cardinal finding which can establish the diagnosis of olmesartan-induced injury based on histopathology.	2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	A. We should have included no, I think a response to a dechallenge with of ARB is probably more meaningful. Q. So if you were to rewrite that sentence, how would it be rewritten consistent with your opinions today? A. I would probably say something to the effect of, ultimately, the history of ARB use with improvement of clinical symptoms following ARB dechallenge is the most meaningful discriminator between celiac disease and ARB enteropathy. And we could go on. Certainly seronegativity and lack of a response to a gluten-free diet do add further supportive evidence. Q. Earlier just so I'm sure I'm understanding, seronegativity and lack of response to a gluten diet don't

Page 234 Page 236 1 response to a gluten-free diet? anything, but let me look at it in more Q. Uh-hum. detail and see --A. You would be describing 3 O. Please. zebras amongst zebras -- sorry. That's 4 (Pause.) sort of medical jargon to say the rarest 5 THE WITNESS: I think since of the rare. And I'm not sure how you 6 I've written this paper, I've seen 7 make the diagnosis -- if the person has 7 more cases of what I believe to be ⁸ never had positive celiac antibody 8 olmesartan enteropathy that look a 9 testing and has never responded to a 9 little bit more like Crohn's gluten-free diet, I'm not sure how you 10 disease than I had seen when I 11 could ever confidently state that they 11 wrote this. 12 have celiac disease. 12 So I might have been -- I 13 Q. My question -- I'm not sure 13 might have worded that part a 14 I got an answer to it -- is, in a person 14 little bit differently. 15 who does not have a positive result of 15 BY MR. PARKER: 16 the antibodies for celiac disease, 16 Q. How would you change it seronegativity, and who does not respond 17 today? 18 to gluten, does that in and of itself, 18 A. I would probably add those two factors, rule out celiac something like a -- like a caveat saying 20 disease? that patchy involvements and granulomas 21 MR. SLATER: Objection. He can occasionally be seen in ARB 22 just answered the question. enteropathy. 23 You can answer it again. 23 Q. Doctor, down at the bottom 24 THE WITNESS: Effectively. ²⁴ of conclusions you wrote, "The mechanism Page 235 Page 237 BY MR. PARKER: of injury is not well established." Do What is refractory celiac you stand by that statement today? 3 disease? A. Well, I think that it's an Refractory celiac disease is immune-mediated inflammatory disorder and a complication, a very rare complication. I think that we've seen that pretty --6 of celiac disease, wherein patients stop pretty consistently in the literature. responding to a gluten-free diet. I think that there has been Q. And seronegative celiac some advancement as far as molecular disease, what is that? mechanism, be it IL15, but I think that 10 A. That's a celiac disease increased CD8+ T cells have been pretty 11 patient who never had a positive celiac convincingly described in the literature, antibody test. so I think that we do know it's an 13 13 immune-mediated inflammatory condition. Q. Doctor, moving down to table ¹⁴ 2 at the bottom, if you were to write Q. So are you saying if you 15 this paper today, would you modify that were writing this paper, you would no 16 table 2 in any manner or does this longer say the mechanism of injury is not 17 reflect your current opinion of the 17 well established? possible histopathologic differences 18 A. I wouldn't use that 19 between ARB enteropathies and other 19 phraseology today. enteropathies? 20 Q. How would you phrase it? 21 21 A. I'll say, first, this is a A. I would say that the 22 table. It's meant to provide easy, quick mechanism of injury involves ²³ access to some information. It's not immune-mediated inflammation and may meant to be an exhaustive list of involve cytokine abnormalities including